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ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: _____

Inventors (please provide full names): NILS CARLIN; PER ASKELOF
ULF BJARE

Earliest Priority Date: 12-18-1998

Search Topic:
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Devi, S.
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Set Items Description - key terms
S1 3657 (ENTEROTOX? OR ENTERO(W)TOXIGEN?)(3N)COLI OR ETEC
S2 574 CFA1 OR CFA2 OR CFA4 OR CFAI OR CFAII OR CFAIV OR (CFA OR (COLONIS? OR COLONIZ? OR COLONY)(W)FACTOR(W)ANTIGEN)(2W)(1 OR I OR 2 OR II OR IV OR 4)
S3 9496 CS1 OR CS2 OR CS3 OR CS4 OR CS5 OR CS6 OR (CS OR SURFACE(W)ANTIGEN)(W)(1 OR 2 OR 3 OR 4 OR 5 OR 6) OR SBL101 OR SBL106 OR SBL107 OR SBL104 OR SBL105 OR SBL(W)(101 OR 106 OR 107 OR 104 OR 105)
S4 101 S2(S)S3
S5 96 S1 AND S4
S6 33 S5 AND ((LT OR ST)(S)(ENTEROTOXIN? ? OR TOXIN? ?) OR HEAT(W)(LABILE OR STABLE) OR CTB OR CHOLERA(3N)B)
S7 29 RD (unique items)
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7/3,AB/1 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
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16272784 Document Delivery Available: 000183100200012 References: 47
TITLE: Mucosal immunization of BALB/c mice using **enterotoxigenic** Escherichia **coli** colonization factors CFA/I and **CS6** administered with and without a mutant **heat-labile** enterotoxin
AUTHOR(S): Byrd W (REPRINT); Cassels FJ
AUTHOR(S) E-MAIL: wyatt.byrd@na.amedd.army.mil
CORPORATE SOURCE: Walter Reed Army Inst Res, Dept Enter Infect, 503 Robert Grant Ave/Silver Spring//MD/20910 (REPRINT); Walter Reed Army Inst Res, Dept Enter Infect, /Silver Spring//MD/20910
PUBLICATION TYPE: JOURNAL
PUBLICATION: VACCINE, 2003, V21, N17-18 (MAY 16), P1884-1893
GENUINE ARTICLE#: 682PF
PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
ISSN: 0264-410X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Mice (BALB/c) were intranasally (IN) and intragastrically (IG)

administered the **ETEC** colonization factors (CF), CFA/I and **CS6**, with and without the R192G mutant **heat-labile** enterotoxin (mLT), and immunogenicity and efficacy measured. The IN administration of **CFA/I** to mice induced strong serum and fecal IgG and IgA responses. The IG administration of **CFA/I** to mice induced serum IgG and fecal IgA responses, but only when mLT was co-administered with **CFA/I** were serum IgA titers detected. The IN administration of **CS6** to mice induced serum IgG antibodies, and mLT, when co-administered with **CS6**, enhanced the serum IgG response. Only when the mLT was co-administered with **CS6**, were serum and fecal IgA responses detected. The IG administration of **CS6** plus mLT induced serum IgG and fecal IgA responses. Partial protection against lethal challenge with **ETEC** strain H10407 was seen in the mice IN administered the **CFA/I** plus mLT ($P < 0.01$), and H10407 was cleared from the lungs of **CFA/I** plus mLT-immunized mice at a significantly greater rate than from the control mice ($P < 0.05$). **CFA /I** and **CS6** administered IN and IG induced mixed Th1/Th2 immune responses with the Th2 type being predominant as evidenced by IgG1 > IgG2a. The administration of colonization factors to mice, particularly by the IN route, potentially serves as a useful way to measure the serum and mucosal immune responses to these antigens prior to their use in volunteers.

7/3,AB/2 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

16272735 Document Delivery Available: 000183100600025 References: 20
TITLE: Safety and immunogenicity of an oral, inactivated **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B** subunit vaccine in Bangladeshi children 18-36 months of age
AUTHOR(S): Qadri F (REPRINT); Ahmed T; Ahmed F; Sack RB; Sack DA; Svennerholm AM
AUTHOR(S) E-MAIL: fqadri@icddrb.org
CORPORATE AUTHOR(S): PTE Study Grp
CORPORATE SOURCE: Int Ctr Diarrhoeal Dis Res, Div Sci Lab, GPO Box 128/Dhaka 1000//Bangladesh/ (REPRINT); Int Ctr Diarrhoeal Dis Res, Div Sci Lab, /Dhaka 1000//Bangladesh/; Johns Hopkins Univ, Dept Int Hlth, /Baltimore//MD/; Gothenburg Univ, Dept Med Microbiol & Immunol, /S-41346 Gothenburg//Sweden/
PUBLICATION TYPE: JOURNAL
PUBLICATION: VACCINE, 2003, V21, N19-20 (JUN 2), P2394-2403
GENUINE ARTICLE#: 682PK
PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
ISSN: 0264-410X
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: A phase II safety and immunogenicity study of an oral-formalin inactivated **enterotoxigenic** Escherichia **coli** (**ETEC**) vaccine containing six colonization factors (CFA/I, **CS1**, **CS2**, **CS3**, **CS4**, **CS5**) and 1 mg of recombinant **cholera** toxin **B** subunit (the CF-BS-**ETEC** vaccine) was carried out in an urban slum of Dhaka city in Bangladesh. The study was carried out in a double blinded, placebo controlled design in 158 children, 18-36 mosnths of age. Children were given two doses of the CF-BS-**ETEC** vaccine or the

placebo which consisted of E. coli K12. The vaccine was well tolerated.

The immune response was studied in 60 children (30 each in the placebo and vaccine group). Significant vaccine specific IgA antibody-secreting cell (ASC) responses were seen 7 days after ingestion of the first and second dose of the vaccine. The responses to CFA/I (P less than or equal to 0.001), **CS2** (P = 0.021), **CS4** (P = 0.009) and rCTB (P less than or equal to 0.001) were elevated in the vaccines in comparison to the pre-immune values and in comparison to those seen in the placebo recipients (P = 0.018 to <0.001). Vaccines but not placebo recipients also showed significantly increased IgM ASC responses to all three CF antigens that were tested (P = 0.012 to <0.001) and IgG-ASCs to rCTB (P < 0.001). Peak ASC levels were reached after one dose of the vaccine with no further increase or decrease after the second dose.

The vaccine recipients also responded with IgA plasma antibodies to CFA/I, **CS1**, **CS2**, **CS4** and rCTB after one or two doses of the vaccine (P = 0.01 to <0.001). Subjects in the placebo group failed to mount responses to any of the antigens. The vaccine also induced responses in mucosal IgA antibodies in feces to **CFA/I**, **CS2** and rCTB (61, 88 and 69% responder frequency, respectively) and the magnitude of the response was elevated in comparison to the pre-immune levels (P = 0.031 to <0.001) and to the levels of the control group (P = 0.003 to <0.001). This study thus shows that the CF-BS-**ETEC** vaccine is well tolerated in children, 18-36 months of age and gives rise to significant systemic and mucosal IgA antibody responses.

7/3,AB/3 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

15746555 Document Delivery Available: 000181429700002 References: 51
TITLE: Development and evaluation of genotypic assays for the detection and characterization of **enterotoxigenic** Escherichia **coli**
AUTHOR(S): Steinsland H (REPRINT); Valentiner-Branth P; Grewal HMS; Gaastra W; Molbak K; Sommerfelt H
AUTHOR(S) E-MAIL: hans.steinsland@bio.uib.no
CORPORATE SOURCE: Univ Bergen, Ctr Int Hlth, Armauer Hansen Bldg/N-5021 Bergen//Norway/ (REPRINT); Univ Bergen, Ctr Int Hlth, /N-5021 Bergen//Norway/; Statens Serum Inst, Danish Epidemiol Sci Ctr, /DK-2300 Copenhagen//Denmark/; Univ Bergen, Dept Microbiol & Immunol, /N-5021 Bergen//Norway/; Haukeland Hosp, /N-5021 Bergen//Norway/; Univ Utrecht, Inst Infect Dis & Immunol, /NL-3508 TC Utrecht//Netherlands/
PUBLICATION TYPE: JOURNAL
PUBLICATION: DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE, 2003, V45, N2 (FEB), P97-105
GENUINE ARTICLE#: 653HT
PUBLISHER: ELSEVIER SCIENCE INC, 360 PARK AVE SOUTH, NEW YORK, NY 10010-1710 USA
ISSN: 0732-8893
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: We developed and evaluated a method to genotypically identify **enterotoxigenic** Escherichia **coli** (**ETEC**) and to characterize these organisms with respect to 18 of 21 known colonization factors (CFs). The method, which is based on polynucleotide DNA-DNA colony

hybridization, includes a pooled **toxin** probe assay to identify **ETEC**, and individual probe assays to detect the **enterotoxins** STp, STh, and **LT**, and the Us CFA/I, **CS1**-CS8, CS12-CS15, CS17-CS19, CS21, and CS22. We evaluated the pooled **toxin** probe assay during a cohort study of childhood diarrhea, and the individual probe assays against 33 reference strains and 92 clinical **ETEC** isolates. There was close to a complete agreement between the pooled **toxin** probe assay and the individual **toxin** probe assays, and between the individual CF probe assays and the corresponding phenotypic assays.

7/3,AB/4 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

15590091 Document Delivery Available: 000180956400002 References: 40
TITLE: Immune responses elicited against multiple **enterotoxigenic** Escherichia **coli** fimbriae and mutant LT expressed in attenuated Shigella vaccine strains
AUTHOR(S): Barry EM (REPRINT); Altboum Z; Losonsky G; Levine MM
AUTHOR(S) E-MAIL: ebarry@umaryland.edu
CORPORATE SOURCE: Univ Maryland, Ctr Vaccine Dev, 685 W Baltimore St/Baltimore//MD/21201 (REPRINT); Univ Maryland, Ctr Vaccine Dev, /Baltimore//MD/21201; Israel Inst Biol Res, Dept Infect Dis, /IL-74100 Ness Ziona//Israel/
PUBLICATION TYPE: JOURNAL
PUBLICATION: VACCINE, 2003, V21, N5-6 (JAN 17), P333-340
GENUINE ARTICLE#: 645BM
PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
ISSN: 0264-410X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Shigella and **enterotoxigenic** Escherichia **coli** (**ETEC**) continue to be important causes of diarrheal disease in infants and young children in developing countries and are major etiologic agents of traveler's diarrhea. Since attenuated strains of Shigella have been developed as live oral vaccines against shigellosis, we have adapted these attenuated Shigella strains to serve as carriers of **ETEC** antigens, thereby constituting a hybrid vaccine. Since protective immunity against **ETEC** is largely directed against fimbrial antigens (of which there are multiple antigenic types), we have individually expressed four different **ETEC** fimbriae, including CFA/I, **CS2**, **CS3**, and **CS4**, using DeltaguaBA attenuated Shigella vaccine strain CVD 1204 as a prototype live vector. Following mucosal (intranasal) immunization of guinea pigs, serum IgG and mucosal IgA responses were elicited against each fimbrial type. An additional strain was constructed expressing a detoxified version of the human **ETEC** variant of **heat labile** toxin (LThK63). Following mucosal immunization of guinea pigs with a mixed inoculum containing five Shigella strains each expressing a different **ETEC** antigen, immune responses were observed against each **ETEC** antigen plus the Shigella vector. (C) 2002 Elsevier Science Ltd. All rights reserved.

7/3,AB/5 (Item 5 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

15399231 Document Delivery Available: 000180212000002 References: 51
TITLE: Pathogenicity and immune response measured in mice following intranasal challenge with **enterotoxigenic** Escherichia **coli** strains H10407 and B7A
AUTHOR(S): Byrd W (REPRINT); Mog SR; Cassels FJ
AUTHOR(S) E-MAIL: wyatt.byrd@na.amedd.army.mil
CORPORATE SOURCE: Walter Reed Army Inst Res, Dept Enter Infect, 503 Robert Grant Ave/Silver Spring//MD/20910 (REPRINT); Walter Reed Army Inst Res, Dept Enter Infect, /Silver Spring//MD/20910; Walter Reed Army Inst Res, Dept Comparat Pathol, /Silver Spring//MD/20910
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 2003, V71, N1 (JAN), P13-21
GENUINE ARTICLE#: 632EZ
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The pathogenicity and immunogenicity induced in BALB/c mice by intranasal (i.n.) inoculation of **enterotoxigenic** Escherichia **coli** (**ETEC**) strains H10407 (078:H11:CFA/I:**LT**+:**ST**+) and B7A (0148:H28:**CS6**:**LT**+: **ST**+) (two **ETEC** strains previously used in human challenge trials) were studied. The i.n. inoculation of BALB/c mice with large doses of **ETEC** strains H10407 and B7A caused illness and death. The H10407 strain was found to be consistently more virulent than the B7A strain. Following i.n. challenge with nonlethal doses of H10407 and B7A, the bacteria were cleared from the lungs of the mice at a steady rate over a 2-week period. Macrophages and neutrophils were observed in the alveoli and bronchioles, and lymphocytes were observed in the septa, around vessels, and in the pleura of the lungs in mice challenged with H10407 and B7A. In mice i.n. challenged with H10407, serum immunoglobulin G (IgG) and IgM antibodies were measured at high titers to the **CFA/I** and 078 lipopolysaccharide (LPS) antigens. In mice i.n. challenged with B7A, low serum IgG antibody titers were detected against **CS6**, and low serum IgG and IgM antibody titers were detected against 0148 LPS. The serum IgG and IgM antibody titers against the **heat-labile enterotoxin** were equivalent in the H10407- and B7A-challenged mice. The **CFA/I** and 078 LPS antigens gave mixed T-helper cell I-T-helper cell 2 (Th1-Th2) responses in which the Th2 response was greater than the Th1 response (i.e., stimulated primarily an antibody response). These studies indicate that the i.n. challenge of BALB/c mice with **ETEC** strains may provide a useful animal model to better understand the immunogenicity and pathogenicity of **ETEC** and its virulence determinants. This model may also be useful in providing selection criteria for vaccine candidates for use in primate and human trials.

7/3,AB/6 (Item 6 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

14254441 Document Delivery Available: 000176605800045 References: 29
TITLE: Prevalence of **enterotoxigenic** Escherichia **coli** strains harboring the longus pilus gene in Brazil
AUTHOR(S): Nishimura LS; Giron JA (REPRINT); Nunes SL; Guth BEC
AUTHOR(S) E-MAIL: jagiron@yahoo.com
CORPORATE SOURCE: Benemerita Univ Autonoma Puebla, Ctr Invest Ciencias Microbiol, Edificio 76 Complejo Ciencas,Ciudad Univ/Puebla//Mexico/ (REPRINT); Benemerita Univ Autonoma Puebla, Ctr Invest Ciencias Microbiol, /Puebla//Mexico/; Univ Fed Sao Paulo, Dept Microbiol Imunol & Parasitol, /Sao Paulo//Brazil/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF CLINICAL MICROBIOLOGY, 2002, V40, N7 (JUL), P 2606-2608
GENUINE ARTICLE#: 569MH
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 0095-1137
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The longus type IV pilus gene (IngA) was highly prevalent (32.8%) among Brazilian **enterotoxigenic** Escherichia **coli** strains producing both **heat-labile** and **heat-stable** enterotoxins and bearing the CFA/I, CS1CS3, or **CS6** antigen. Furthermore, IngA was more often found in strains isolated from children with diarrhea than in strains isolated from children without diarrhea.

7/3,AB/7 (Item 7 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

13831237 Document Delivery Available: 000175150500011 References: 35
TITLE: Introductory evaluation of an oral, killed whole cell **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B** subunit vaccine in Egyptian infants
AUTHOR(S): Savarino SJ (REPRINT); Hall ER; Bassily S; Wierzba TF; Youssef FG; Peruski LF; Abu-Elyazeed R; Rao M; Francis WM; El Mohamady H; Safwat M; Naficy AB; Svennerholm AM; Jertborn M; Lee YJ; Clemens JD
AUTHOR(S) E-MAIL: savarinos@nmrc.navy.mil
CORPORATE AUTHOR(S): Pride Study Grp
CORPORATE SOURCE: USN, Med Res Ctr, 503 Robert Grant Ave/Silver Spring//MD/20910 (REPRINT); USN, Med Res Unit 3, /Cairo//Egypt/; Egyptian Minist Hlth & Populat, Al Qalyubiyah Governorate, /Banha//Egypt/; NICHHD, Div Epidemiol Stat & Prevent Res, /Bethesda//MD/20892; Univ Gothenburg, Dept Med Microbiol & Immunol, /Gothenburg//Sweden/; Int Vaccine Inst, /Seoul//South Korea/
PUBLICATION TYPE: JOURNAL
PUBLICATION: PEDIATRIC INFECTIOUS DISEASE JOURNAL, 2002, V21, N4 (APR), P 322-330
GENUINE ARTICLE#: 544GU
PUBLISHER: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621 USA
ISSN: 0891-3668
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Background. We conducted the first trial to assess the safety and

immunogenicity of an oral, killed **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B**-subunit vaccine in children <2 years old.

Methods. Three doses of vaccine or killed E. coli K-12 control were given at 2-week intervals to 64 Egyptian infants, 6 to 18 months old, in a randomized, double blind manner. Adverse events were monitored for 3 days after each dose. Blood was collected before immunization and 7 to 10 days after each dose to assess vaccine-specific serologic responses.

Results. There was no statistically significant intergroup difference in the percentage of subjects reporting the primary safety endpoint (diarrhea or vomiting) after the first (31%, vaccine; 30%, control) or third (14%, vaccine; 18%, control) dose, whereas there was a trend toward greater reporting in the vaccine group after Dose 2 (36%, vaccine; 18%, control; P = 0.052). The percentage of children showing IgA seroconversion after any dose was higher in the vaccine than the control group for recombinant **cholera** toxin **B**-subunit (97% vs. 46%), colonization factor antigen 1 (61% vs. 18%) and coli **surface antigen 4** (39% vs. 4%) (P < 0.001 for each comparison). IgG seroconversion rates in the vaccine and control groups were 97 and 21% to recombinant **cholera** toxin **B**-subunit (P < 0.001), 64 and 29% for **colonization factor antigen I** (P < 0.01), 53 and 21% for coli **surface antigen 2** (P < 0.05) and 58 and 4% for coli **surface antigen 4** (P < 0.001), respectively. The third vaccine dose was followed by augmented IgG antitoxin titers.

Conclusion. The oral **enterotoxigenic** E. **coli** vaccine was safe and immunogenic in this setting in Egyptian infants.

7/3,AB/8 (Item 8 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12946372 References: 38
TITLE: Toxins and colonization factor antigens of **enterotoxigenic** Escherichia **coli** among residents of Jakarta, Indonesia
AUTHOR(S): Oyofo BA (REPRINT); Subekti DS; Svennerholm AM; Machpud NN; Tjaniadi P; Komalarini S; Setiawan B; Campbell JR; Corwin AL; Lesmana M
CORPORATE SOURCE: USN, Med Res Unit 2, /Jakarta//Indonesia/ (REPRINT); USN, Med Res Unit 2, /Jakarta//Indonesia/; Gothenburg Univ, Dept Med Microbiol & Immunol, /Gothenburg//Sweden/; Friendship Hosp, /Jakarta//Indonesia/; Sumber Waras Hosp, /Jakarta//Indonesia/
PUBLICATION TYPE: JOURNAL
PUBLICATION: AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE, 2001, V65, N2 (AUG), P120-124
GENUINE ARTICLE#: 461ML
PUBLISHER: AMER SOC TROP MED & HYGIENE, 8000 WESTPARK DR, STE 130, MCLEAN, VA 22101 USA
ISSN: 0002-9637
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Infection caused by **enterotoxigenic** Escherichia **coli** (**ETEC**) poses a serious health problem among children and adults in developing countries. Colonization of the small intestinal mucosa by

ETEC strains is mediated by antigenically specific fimbriae, also known as colonization factor antigens (CFA). The significance of this study arises from reports that active and passive immunization with **ETEC** strains harboring CFAs has previously been shown to induce protective immunity against diarrhea in animal models. The aim of this study was to determine **toxin**-associated CFAs of **ETEC** isolated from a diarrheal disease case-control study in Jakarta, Indonesia. Thirteen hundred and twenty-three diarrheic and control patients with lactose-fermenting colonies were screened by ganglioside GM1-enzyme-linked immunosorbent assay (GM1-ELISA) for **heat-labile** (**LT**) and **heat-stable** (**ST**) **toxins**. Two hundred and forty-six (19%) **ETEC** isolates identified by GM1-ELISA for the **LT/ST toxins** were screened for CFAs by Dot blot assay using monoclonal antibodies against CFA/I, II, and IV and against the putative colonization antigens (PCF) PCFO159, PCFO166, CS7, and CS17 Of the 246 **ETEC** isolates, 177 (72%) elaborated **ST**, 56 (23%) produced **LT**, while 13 (5%) elicited both the **ST** and **LT toxins**. CFA testing of the 246 **ETEC** isolates showed that 21 (8%) expressed CFA/I, 3 (1%) exhibited CFA/II, 14 (6%) elaborated CFA/IV, while 7 (3%) expressed PCFO159 and PCFO159 plus **CS5**. No CFAs or PCFs could be associated with 201 (82%) of the **ETEC** strains. This report documents the types of CFAs associated with **ETEC** strains in Jakarta, Indonesia. These data may help cur-rent research efforts on the development of CFA-based vaccines for humans against **ETEC** and provide additional information for future **ETEC** vaccine trials in Southeast Asia.

7/3,AB/9 (Item 9 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12618961 References: 21
TITLE: Induction of systemic antifimbria and antitoxin antibody responses in Egyptian children and adults by an oral, killed **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B** subunit vaccine
AUTHOR(S): Hall ER; Wierzba TF; Ahren C; Rao MR; Bassily S; Francis W; Girgis FY; Safwat M; Lee YJ; Svennerholm AM; Clemens JD; Savarino SJ (REPRINT)
AUTHOR(S) E-MAIL: savarinos@nmrc.navy.mil
CORPORATE SOURCE: USN, Enter Dis Dept, 503 Robert Grant Ave/Silver Spring//MD/20910 (REPRINT); USN, Med Res Unit 3, /Cairo//Egypt/; Egyptian Minist Hlth & Populat, /Benha/Qalyubia Govern/Egypt/; Univ Gothenburg, Dept Med Microbiol & Immunol, /Gothenburg//Sweden/; NICHHD, Div Epidemiol Stat & Prevent Res, /Bethesda//MD/20892
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 2001, V69, N5 (MAY), P2853-2857
GENUINE ARTICLE#: 423CT
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: We assessed serologic responses to an oral, killed whole-cell **otoxigenic** Escherichia **coli** plus **cholera** toxin unit (**ETEC**-rCTB) vaccine in 73 Egyptian adults, 105

schoolchildren, and 93 preschool children. Each subject received two doses of vaccine or placebo 2 weeks apart, giving blood before immunization and 7 days after each dose. Plasma antibodies to rCTB and four vaccine-shared colonization factors (CFs) were measured by enzyme-linked immunosorbent assay. Immunoglobulin A (IgA) antibodies to rCTB and CFA/I were measured in all subjects, and those against **CS1**, **CS2**, and **CS4** were measured in all children plus a subset of 33 adults. IgG antibodies to these five antigens were measured in a subset of 30 to 33 subjects in each cohort. Seroconversion was defined as a >2-fold increase in titer after vaccination. IgA and IgG seroconversion to rCTB was observed in 94 to 95% of adult vaccinees, with titer increases as robust as those previously reported for these two pediatric cohorts. The proportion showing IgA seroconversion to each CF antigen among vaccinated children (range, 70 to 96%) and adults (31 to 69%), as well as IgG seroconversion in children (44 to 75%) and adults (25 to 81%), was significantly higher than the corresponding proportion in placebo recipients, except for IgA responses to **CS2** in adults. IgA anti-CF titers peaked after one dose in children, whereas in all age groups IgG antibodies rose incrementally after each dose. Independently, both preimmunization IgA titer and age were inversely related to the magnitude of IgA responses. In conclusion, serologic responses to the **ETEC** rCTB vaccine mag serve as practical immune outcome measures in future pediatric trials in areas where **ETEC** is endemic.

7/3,AB/10 (Item 10 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12499517 References: 23
TITLE: Dose-dependent circulating immunoglobulin A antibody-secreting cell and serum antibody responses in Swedish volunteers to an oral inactivated **enterotoxigenic** Escherichia **coli** vaccine
AUTHOR(S): Jertborn M (REPRINT); Ahren C; Svennerholm AM
AUTHOR(S) E-MAIL: marianne.jertborn@microbio.gu.se
CORPORATE SOURCE: Gothenburg Univ, Dept Med Microbiol & Immunol, Guldhedsgatan 10/S-41346 Gothenburg//Sweden/ (REPRINT); Gothenburg Univ, Dept Med Microbiol & Immunol, /S-41346 Gothenburg//Sweden/; Gothenburg Univ, Dept Infect Dis, /S-41346 Gothenburg//Sweden/
PUBLICATION TYPE: JOURNAL
PUBLICATION: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, 2001, V8, N2 (MAR), P424-428
GENUINE ARTICLE#: 409FF
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 1071-412X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The immunogenicity of different preparations of an oral inactivated **enterotoxigenic** Escherichia **coli** (**ETEC**) vaccine was evaluated in Swedish volunteers previously unexposed to **ETEC** infection. The vaccine prepara tions consisted of recombinant **cholera** toxin **B** subunit (**CTB**) and various amounts of formalin-killed whole bacteria expressing the most prevalent colonization factor antigens (CFAs). Significant immunoglobulin A (IgA) antibody-secreting cell (ASC) responses against **CTB** and the various

CFA components were seen in a majority of volunteers after two doses of **ETEC** vaccine independent of the vaccine lot given. The IgA ASC responses against **CTB** were significantly higher after the second than after the first immunization, whereas the CFA-specific IgA ASC responses were almost comparable after the first and second doses of **ETEC** vaccine. Two immunizations with one-third of a full dose of CFA-**ETEC** bacteria induced lower frequencies of IgA ASC responses against all the different CFAs than two full vaccine doses, i,e., 63 versus 80% for CFA/I, 56 versus 70% for **CS1**, 31 versus 65% for **CS2**, and 56 versus 75% for **CS4**. The proportion of vaccinees responding with rises in the titer of serum IgA antibody against the various CFA antigens was also lower after immunization with the reduced dose of CFA-**ETEC** bacteria. These findings suggest that measurements of circulating IgA ASCs can be used not only for qualitative but also for quantitative assessments of the immunogenicity of individual fimbrial antigens in various preparations of **ETEC** vaccine.

7/3,AB/11 (Item 11 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

11840143 References: 18
TITLE: Safety and immunogenicity of two different lots of the oral, killed **enterotoxigenic** Escherichia **coli cholera** toxin **B** subunit vaccine in Israeli young adults
AUTHOR(S): Cohen D; Orr N; Haim M; Ashkenazi S; Robin G; Green MS; Ephros M; Sela T; Slepon R; Ashkenazi I; Taylor DN; Svennerholm AM; Eldad A; Shemer J
AUTHOR(S) E-MAIL: danic@netvision.net.il
CORPORATE SOURCE: Tel Aviv Univ, Sackler Fac Med, /IL-69978 Tel Aviv//Israel/; Technion Israel Inst Technol, Bruce Rappaport Fac Med, /Haifa//Israel/; Ben Gurion Univ Negev, Fac Hlth Sci, /Beer Sheva//Israel/; Hebrew Univ Jerusalem, /Jerusalem//Israel/; Hadassah Med Sch, /Jerusalem//Israel/; Univ Gothenburg, /Gothenburg//Sweden/; Walter Reed Army Inst Res, /Washington//DC/
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 2000, V68, N8 (AUG), P4492-4497
GENUINE ARTICLE#: 337AY
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Enterotoxigenic Escherichia coil (**ETEC**) is one of the leading causes of diarrhea among Israeli soldiers serving in field units. Two double-blind placebo-controlled, randomized trials were performed among 155 healthy volunteers to evaluate the safety and immunogenicity of different lots of the oral, killed **ETEC** vaccine consisting of two doses of whole cells plus recombinantly produced **cholera** toxin **B** subunit (rCTB). The two doses of vaccine lot E005 and the first dose of vaccine lot E003 were well tolerated by the volunteers. However, 5 (17%) vaccinees reported an episode of vomiting a few hours after the second dose of lot E003; none of the placebo recipients reported similar symptoms. Both lots of vaccine stimulated a rate of significant ibody-secreting cell (ASC) response to **CTB** and to colonization

factor antigen I (CFA/I) after one or two doses, ranging from 85 to 100% and from 81 to 100%, respectively. The rate of ASC response to **CS2**, **CS4**, and **CS5** was slightly lower than the rate of ASC response induced to **CTB**, **CFA/I**, and **CS1**. The second vaccine dose enhanced the response to **CTB** but did not increase the frequencies or magnitude of ASC responses to the other antigens. The two lots of the **ETEC** vaccine induced similar rates of serum antibody responses to **CTB** and **CFA/I** which were less frequent than the ASC responses to the same antigens. Based on these safety and immunogenicity data, an efficacy study of the **ETEC** vaccine is under way in the Israel Defense Force.

7/3,AB/12 (Item 12 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

11254296 References: 27
TITLE: Prevalence of toxin types and colonization factors in **enterotoxigenic** Escherichia **coli** isolated during a 2-year period from diarrheal patients in Bangladesh
AUTHOR(S): Qadri F (REPRINT); Das SK; Faruque ASG; Fuchs GJ; Albert MJ; Sack RB; Svennerholm AM
AUTHOR(S) E-MAIL: fqadri@icddrb.org
CORPORATE SOURCE: ICDDR B, Div Sci Lab, GPO Box 128/Dhaka 1000//Bangladesh/ (REPRINT); ICDDR B, Div Sci Lab, /Dhaka 1000//Bangladesh/; Johns Hopkins Univ, Dept Int Hlth, /Baltimore//MD/; Gothenburg Univ, Dept Med Microbiol & Immunol, /S-41346 Gothenburg//Sweden/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF CLINICAL MICROBIOLOGY, 2000, V38, N1 (JAN), P27-31
GENUINE ARTICLE#: 273CN
PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171 USA
ISSN: 0095-1137
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The prevalence of **toxin** types and colonization factors (CFs) of **enterotoxigenic** Escherichia **coli** (**ETEC**) was prospectively studied with fresh samples (n = 4,662) obtained from a 2% routine surveillance of diarrheal stool samples over 2 years, from September 1996 to August 1998, Stool samples were tested by enzyme-linked immunoassay techniques and with specific monoclonal antibodies for the **toxins** and CFs. The prevalence of **ETEC** was 14% (n = 662), with over 70% of the strains isolated from children 0 to 5 years of age, of whom 93% were in the 0- to 3-year-old age range. Of the total **ETEC** isolates, 49.4% were positive for the **heat-stable toxin** (**ST**), 25.4%, were positive for the **heat-labile toxin** (**LT**) only, and 25.2% were positive for both **LT** and **ST**, The rate of **ETEC** isolation peaked in the hot summer months of May to September and decreased in winter. About 56% of the samples were positive for 1 or more of the 12 CFs that were screened for. The coli surface antigens CS4, CS5, and/or CS6 of the colonization factor antigen (CFA)ITV complex were most prevalent (incidence, 31%), followed by CPA/I (23.5%) and coli surface antigens CS1, CS2, and CS3 of **CFA/II** (21%). In addition, other CFs detected in decreasing order were CS7 (8%), CS14 (PCFO166) (7%), CS12 (PCFO159) (4%), CS17 (3%), and CS8 (**CFA**/III) (

2.7%), The **ST**- or **LT**- and **ST**-positive **ETEC** isolates expressed the CFs known to be the most prevalent (i.e., **CFA/I, CFA/II,** and **CFA/IV**), while the strains positive for **LT** only did not. Among children who were infected with **ETEC** as the single pathogen, a trend of relatively more severe disease in children infected with **ST**-positive ($P < 0.001$) or **LT** - and **ST**-positive ($P < 0.001$) **ETEC** isolates compared to the severity of the disease in children infected with **LT** only-positive **ETEC** isolates was seen. This study supports the fact that **ETEC** is still a major cause of childhood diarrhea in Bangladesh, especially in children up to 3 years of age, and that measures to prevent such infections are needed in developing countries.

7/3,AB/13 (Item 13 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

10760424 References: 46
TITLE: Characterization of an **enterotoxigenic** Escherichia **coli** strain from Africa expressing a putative colonization factor
AUTHOR(S): Khalil SB; Cassels FJ; Shaheen HI; Pannell LK; El-Ghorab N; Kamal K; Mansour M; Savarino SJ; Peruski LF (REPRINT)
AUTHOR(S) E-MAIL: boushrah@namru3.navy.mil
CORPORATE SOURCE: USN, Med Res Unit 3, PSC 452,Box 5000/FPO//AE/09835 (REPRINT); USN, Res Sci Dept, /Cairo//Egypt/; Walter Reed Army Med Ctr, Dept Enter Infect, /Washington//DC/20307; NIDDKD, NIH, /Bethesda//MD/20892
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 1999, V67, N8 (AUG), P4019-4026
GENUINE ARTICLE#: 219ZA
PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171 USA
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: An **enterotoxigenic** Escherichia **coli** (**ETEC**) strain of serotype O114:H- that expressed both **heat-labile** and **heat-stable** enterotoxins and tested negative for colonization factors (CF) was isolated from a child with diarrhea in Egypt. This strain, WS0115A, induced hemagglutination of bovine erythrocytes and adhered to the enterocyte-like cell line Caco-2, suggesting that it may elaborate novel fimbriae. Surface-expressed antigen purified by differential ammonium sulfate precipitation and column chromatography yielded a single protein band with M-r 14,800 when resolved by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (16% polyacrylamide). A monoclonal antibody against this putative fimbrial antigen was generated and reacted with strain WS0115A and also with CS1-, CS17-, and CS19-positive strains in a dot blot assay. Reactivity was temperature dependent, with cells displaying reactivity when grown at 37 degrees C but not when grown at 22 degrees C. Immunoblot analysis of a fimbrial preparation from strain WS0115A showed that the monoclonal antibody reacted with a single protein band. Electron microscopy and immunoelectron microscopy revealed fimbria-like structures on the surface of strain WS0115A. These structures were rigid and measured 6.8 to 7.4 nm in diameter. Electrospray mass-spectrometric analysis showed that the mass of the purified fimbria was 14,965 Da. The N-terminal

sequence of the fimbria established that it was a member of the **CFA/ I** family, with sequence identity to the amino terminus of CS19, a new CF recently identified in India. Cumulatively, our results suggest that this fimbria is CS19. Screening of a collection of **ETEC** strains isolated from children with diarrhea in Egypt found that 4.2% of strains originally reported as CF negative were positive for this CF, suggesting that it is biologically relevant in the pathogenesis of **ETEC**.

7/3,AB/14 (Item 14 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

10138548 References: 38
TITLE: Oral, inactivated, whole cell **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B** subunit vaccine: Results of the initial evaluation in children
AUTHOR(S): Savarino SJ (REPRINT); Hall ER; Bassily S; Brown FM; Youssef F; Wierzba TF; Peruski L; El-Masry NA; Safwat M; Rao M; El Mohamady H; Abu-Elyazeed R; Naficy A; Svennerholm AM; Jertborn M; Lee YJ; Clemens JD
AUTHOR(S) E-MAIL: savarino@namru3.navy.mil
CORPORATE AUTHOR(S): PRIDE Study Grp
CORPORATE SOURCE: USN, Med Res Unit 3, PSC 452,Box 5000/FPO//AE/09835 (REPRINT); USN, Med Res Unit 3, /Cairo//Egypt/; Egyptian Minist Hlth, /Benha//Egypt/; Qalyubia Governorate, /Governorate//Egypt/; NICHHD, NIH, /Bethesda//MD/20892; Gothenburg Univ, Dept Med Microbiol & Immunol, /S-41124 Gothenburg//Sweden/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF INFECTIOUS DISEASES, 1999, V179, N1 (JAN), P107-114
GENUINE ARTICLE#: 151MW
PUBLISHER: UNIV CHICAGO PRESS, 5801 S ELLIS AVENUE, CHICAGO, IL 60637 USA
ISSN: 0022-1899
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: Two randomized, double-blinded trials assessed the safety and immunogenicity of an oral, killed **enterotoxigenic** Escherichia **coli** (**ETEC**) plus **cholera** toxin **B** subunit vaccine in Egyptian children. Two doses of vaccine or E. coli K-12 were given 2 weeks apart to 105 6- to 12-year-olds and 97 2- to 5-year-olds. Safety was monitored for 3 days after each dose. Blood was collected before immunization and 7 days after each dose to measure immune responses. Few children reported postdosing symptoms, with no differences in the frequency of symptoms between treatment groups. Most vaccinees had an IgA antibody-secreting cell response against colonization factor antigen I(100%, 6-12 years; 95%, 2-5 years), coli **surface antigen 2** (92%, 6-12 years; 83%, 2-5 years), and coli **surface antigen 4** (93%, 6-12 years). Vaccination evoked a greater than or equal to 4-fold rise in antitoxic IgA and IgG titers in 93% and 81% of children, respectively, In conclusion, the oral **ETEC** vaccine was safe and immunogenic in 2- to 12-year-old children, justifying further evaluation in infants.

7/3,AB/15 (Item 15 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09831034 References: 48
TITLE: Epidemiology and properties of **heat-stable enterotoxin**-producing Escherichia **coli** serotype O169:H41
AUTHOR(S): Nishikawa Y (REPRINT); Helander A; Ogasawara J; Moyer NP; Hanaoka M; Hase A; Yasukawa A
CORPORATE SOURCE: OSAKA CITY INST PUBL HLTH & ENVIRONM SCI,DEPT EPIDEMIOL, TOJO CHO/OSAKA 5430026//JAPAN/ (REPRINT); GOTHENBURG UNIV,DEPT MED MICROBIOL & IMMUNOL/S-41124 GOTHENBURG//SWEDEN/; UNIV IOWA,HYG LAB/IOWA CITY//IA/52242
PUBLICATION TYPE: JOURNAL
PUBLICATION: EPIDEMIOLOGY AND INFECTION, 1998, V121, N1 (AUG), P31-42
GENUINE ARTICLE#: 118ZW
PUBLISHER: CAMBRIDGE UNIV PRESS, 40 WEST 20TH STREET, NEW YORK, NY 10011-4211
ISSN: 0950-2688
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Enterotoxigenic Escherichia coil (**ETEC**) serotype O169:H41 organisms have become the most prevalent **ETEC** in Japan since the first outbreak in 1991. It was assumed that the outbreaks were due to clonal spread of this new **ETEC** serotype. The relationship of 32 strains isolated from 6 outbreaks were examined for biotype, antibiotic susceptibility, enterotoxigenicity, protein banding pattern, lipopolysaccharide banding pattern, plasmid analysis, and ribotyping. Further, the strains were examined by haemagglutination, surface hydrophobicity, and the ability to adhere to HEp-2 cells. The present study suggests that the outbreaks were caused by multiple clones of STp-producing O169:H41 since they showed differences in ribotype and outer membrane protein banding patterns. The strains did not agglutinate human or bovine red blood cells in a mannose-resistant manner. They adhered to HEp-2 cells in a manner resembling enteroaggregative E. coli. Five strains were examined by dot-blot tests for the colonization factor antigens CFA/I, **CS1**, **CS2**, **CS3**, **CS4**, **CS5**, **CS6**, CS7, PCFO159, PCFO166 and CFA/III. Although four strains expressed **CS6**, no structure for **CS6** was identified. A strain that the anti-**CS6** MAbs did not react with could adhere to HEp-2 cells in mannose resistant manner; thus, it is unlikely that **CS6** play an important role in the adhesion to the cells. Electron microscopy studies of the O169:H41 strains suggested that curly fimbriae, a possible new colonization factor, may be playing an important role in the adhesion of the bacteria to HEp-2 cells. In conclusion, outbreaks due to **ETEC** O169:H41 were caused by multiple clones, and the strains should be examined in detail for a possible new colonization factor.

7/3,AB/16 (Item 16 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09237690 References: 14
TITLE: Safety and immunogenicity of an oral, killed **enterotoxigenic** Escherichia **coli** - **Cholera** toxin **B** subunit vaccine in Egyptian adults
AUTHOR(S): Savarino SJ (REPRINT); Brown FM; Hall E; Bassily S; Youssef F; Wierzba T; Peruski L; ElMasry NA; Safwat M; Rao M; Jertborn M; Svennerholm AM; Lee YJ; Clemens JD

CORPORATE SOURCE: USN,MED RES UNIT 3, PSC 452, BOX 127/FPO//AE/09835 (REPRINT); USN,MED RES UNIT 3/CAIRO//EGYPT/; EQYPTIAN MINIST HLTH,/BANHA//EGYPT/; NICHHD,NIH/BETHESDA//MD/20892; GOTHENBURG UNIV,/GOTHENBURG//SWEDEN/
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF INFECTIOUS DISEASES, 1998, V177, N3 (MAR), P796-799
GENUINE ARTICLE#: YY555
PUBLISHER: UNIV CHICAGO PRESS, 5720 S WOODLAWN AVE, CHICAGO, IL 60637
ISSN: 0022-1899
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: **Enterotoxigenic** Escherichia **coli** (**ETEC**) is the leading cause of bacterial diarrhea in young children in developing countries. The safety and immunogenicity of a killed, oral **ETEC** vaccine consisting of whole cells plus recombinantly produced **cholera** toxin **B** subunit (rCTB) was evaluated in Egypt, which is endemic for **ETEC** diarrhea. Seventy-four healthy Egyptian adults (21-45 years old) were randomized and received two doses of the **ETEC**/rCTB vaccine (E003) or placebo 2 weeks apart. The frequency of adverse events after either dose did not differ by treatment group, and no severe adverse events were reported. After vaccination, peripheral blood IgA B cell responses to **CTB** (100%) and to vaccine colonization factor antigens CFA/I (94%), **CS4** (100%), **CS2** (81%), and **CS1** (69%) were significantly higher than response rates for the placebo group. These favorable results in Egyptian adults indicate that the **ETEC**/rCTB vaccine is a promising candidate for evaluation in younger age groups in this setting.

7/3,AB/17 (Item 17 from file: 440)

09045551 References: 31
TITLE: Safety and immunogenicity of an oral inactivated **enterotoxigenic** Escherichia **coli** vaccine
AUTHOR(S): Jertborn M (REPRINT); Ahren C; Holmgren J; Svennerholm AM
CORPORATE SOURCE: GOTHENBURG UNIV,DEPT MED MICROBIOL, GULDHEDSGATAN 10/S-41346 GOTHENBURG//SWEDEN/ (REPRINT); GOTHENBURG UNIV,DEPT INFECT DIS/S-41346 GOTHENBURG//SWEDEN/
PUBLICATION TYPE: JOURNAL
PUBLICATION: VACCINE, 1998, V16, N2-3 (JAN-FEB), P255-260
GENUINE ARTICLE#: YL616
PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, OXON, ENGLAND OX5 1GB
ISSN: 0264-410X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The safety and immunogenicity of two different lots, 001 and 003, of an oral inactivated **enterotoxigenic** Escherichia **coli** (**ETEC**) vaccine consisting of a mixture of formalin-killed whole bacteria expressing the most prevalent colonisation factor antigens, i.e. CFA/I, CFA/II and CFA/IV and recombinantly produced **cholera B** subunit (rCTB) have been evaluated in Swedish volunteers. Neither of the two vaccine preparations, containing different CFA/II-expressing strains but otherwise identical gave rise to any significant side-effects. Mucosal immune responses, as reflected in antibody-secreting cell (ASC) responses

in peripheral blood, were studied after two doses of vaccine and did not differ significantly for the two vaccine lots. Vaccination induced high levels of **CTB**-specific IgA ASCs in 100% of the volunteers, and significant IgA ASC responses (9- to 36-fold) were noted in 84% of them against CFA/I, in 87% against CFA/II subcomponents **CS1-CS3** and in 91% against **CFA/IV** subfactors **CS4** and/or **CS5**.
The frequencies and magnitudes of CFA IgA ASC responses were similar when giving the vaccine with a 1 or 2 week interval. Results from serological analyses showed that the local IgA responses against CFAs are only infrequently associated with serum antibody titre rises.

7/3,AB/18 (Item 18 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

07248036 References: 34
TITLE: DETECTION OF THE ENTEROAGGREGATIVE ESCHERICHIA **COLI HEAT -STABLE ENTEROTOXIN** 1 GENE SEQUENCES IN **ENTEROTOXIGENIC** E-**COLI** STRAINS PATHOGENIC FOR HUMANS
AUTHOR(S): YAMAMOTO T; EXHEVERRIA P
CORPORATE SOURCE: INT MED CTR JAPAN,RES INST,DEPT INFECT DIS & TROP MED,SHINJUKU KU,1-21-2 TOYAMA/TOKYO//JAPAN/ (Reprint); ARMED FORCES RES INST MED SCI,DEPT BACTERIOL IMMUNOL & MOL GENET/BANGKOK 10400//THAILAND/
PUBLICATION: INFECTION AND IMMUNITY, 1996, V64, N4 (APR), P1441-1445
GENUINE ARTICLE#: UC314
ISSN: 0019-9567
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: The sequence of the enteroaggregative Escherichia **coli enterotoxin** 1 (EAST1) gene was present in most (or all) strains of human-colonizing **enterotoxigenic** E. **coli** (**ETEC**) with colonization factor antigen II (CFA/II) or CFA/IV (**CS6**). The EAST1 gene was also strongly associated with PCF09(+) **ETEC** or **CFA/I+ ETEC** elaborating **heat-labile** enterotoxin (and **heat-stable** enterotoxin I). In contrast, **CFA/I+ ETEC** elaborating **heat-stable** enterotoxin I, CFA/III+ **ETEC**, or CS17(+) **ETEC** exhibited very weak or no association. E. coli from healthy volunteers had no EAST1 gene sequence. A **CFA/I+ ETEC** strain (H10407) possessed multiple copies of the EAST1 gene on the **CFA/I**-encoding plasmid and chromosome. In one **CFA/II+ ETEC** strain, the EAST1 gene was present on the **CFA/II**-encoding plasmid. The EAST1 gene sequences of the **CFA/I+** and **CFA/II+ ETEC** strains were identical to each other and 99.1% homologous to the reported gene sequence of enteroaggregative E. coli. The data indicate that the EAST1 gene is distributed among **ETEC** strains with a case of the presence of multiple copies in a single cell and that this distribution is associated with the adherence factor type.

7/3,AB/19 (Item 19 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

07021585 References: 33
TITLE: COLONIZATION FACTORS OF **ENTEROTOXIGENIC** E-**COLI** (**ETEC**) FROM RESIDENTS OF NORTHERN EGYPT
AUTHOR(S): OYOFO BA; ELETR SH; WASFY MO; PERUSKI L; KAY B; MANSOUR M; CAMPBELL JR; SVENNERHOLM AM; CHURILLA AM; MURPHY JR
CORPORATE SOURCE: USN,MED RES UNIT 3,RES PUBLICAT BRANCH,PSC 452,BOX 5000/FPO//AE/09835 (Reprint); USN,MED RES UNIT 3/CAIRO//EGYPT/
PUBLICATION: MICROBIOLOGICAL RESEARCH, 1995, V150, N4 (NOV), P429-436
GENUINE ARTICLE#: TN149
ISSN: 0944-5013
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Infection caused by **enterotoxigenic** Escherichia **coli** (**ETEC**) poses a serious health problem to children in developing countries. Colonization of the small intestinal mucosa by **ETEC** strains is mediated by antigenically specific fimbriae, also known as colonization factor antigens (CFA). The importance of this study arises from reports that active and passive immunization with **ETEC** strains harboring CFAs induced protective immunity against diarrhea in animal models with preformed antibodies. In humans, **ETEC** containing CFA/I, II, III and IV have been identified. The aim of this study was to define CFAs of **ETEC** isolated in Alexandria, Egypt. One hundred and seven **ETEC** isolates from 132 human residents in Alexandria, Egypt were isolated during a birth cohort study. **ETEC** isolates were screened for **heat labile** (**LT**) and **heat stable** (**ST**) **toxins** using a P-32 oligonucleotide hybridization probe and a GM1 ELISA. These isolates were examined using monoclonal antibodies against CPA/I, II, III, IV, and against the putative colonization antigens PCF0159 and PCF0166, CS 7 and CS 17. CFAs were found in 48% of **ETEC** strains. CFA/I was found in 18% of the strains, CFA/II in 10% and CFA/IV in 14%. CFA III was not found. All fifteen strains expressing CFA/IV expressed **CS6** and produced **ST**. **CFA/IV** was not found in non-**ST** producing strains, while **CFA/I** was absent in **ST** - only producing strains.

7/3,AB/20 (Item 20 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

05762465 References: 40
TITLE: PREVALENCE OF COLONIZATION FACTOR ANTIGENS (CFAS) AND ADHERENCE TO HELA CELLS IN ENTEROTOXIGENIC ESCHERICHIA **COLI** ISOLATED FROM FECES OF CHILDREN IN SAO PAULO
AUTHOR(S): GUTH BEC; AGUIAR EG; GRIFFIN PM; RAMOS SRTD; GOMES TAT
CORPORATE SOURCE: ESCOLA PAULISTA MED,DEPT MICROBIOL IMMUNOL & PARASITOL,RUA BOTUCATU 862/BR-04023062 SAO PAULO/SP/BRAZIL/ (Reprint); CTR DIS CONTROL,CTR INFECT DIS,DIV BACTERIAL & MYCOT DIS,FOODBORNE & DIARRHEAL DIS BRANCH/ATLANTA//GA/30333; HOSP INFANTIL MENINO JESUS/BR-01329 SAO PAULO//BRAZIL/; UNIV SAO PAULO,INST CRIANCA/BR-05403000 SAO PAULO/SP/BRAZIL/
PUBLICATION: MICROBIOLOGY AND IMMUNOLOGY, 1994, V38, N9, P695-701
GENUINE ARTICLE#: PG176
ISSN: 0385-5600
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Fifty-eight **enterotoxigenic** Escherichia **coli** (**ETEC**) strains, isolated from children with and without diarrhea in Sao Paulo, were examined for the presence of colonization factor antigens (CFAs) and their ability to adhere to HeLa cells. Antisera to CFA/I, the coli surface (CS) antigens CS1CS3, CS2CS3, and **CS2** of **CFA/II**, CFA/III, and CS5CS6 and **CS6** of **CFA/IV** were used. CFAs were identified in 43% of the **ETEC** strains: 40% of the strains with CFAs harbored **CFA/I**, 24% carried **CFA/II** (CS1CS3), 24%; carried **CFA/IV** (**CS6**), and 12% carried **CFA/IV** (CS5CS6). CFAs occurred mainly among **ETEC** strains producing only **heat-stable** (**ST**-I) **enterotoxin** and in strains also producing **heat-labile toxin** (**LT**-I). No **ETEC** strains tested expressed CFA/III. A marked change in serotypes of **ST**-I-producing strains was found in Sao Paulo between 1979 and 1990. Adherence to HeLa cells was detected in 14% of the **ETEC** strains. All of them had a diffuse adherence pattern and produced only **ST**-I, and 88% carried **CS6** antigen.

7/3,AB/21 (Item 21 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03832024 References: 25
TITLE: RELATIONSHIP BETWEEN **ENTEROTOXIGENIC** ESCHERICHIA-**COLI** AND DIARRHEA AMONG CHILDREN IN BUENOS-AIRES
AUTHOR(S): BINSZTEIN N; RIVAS M; MORAL LL; VIBOUD G; IRIARTE C; SZEFNER M; SVENNERHOLM AM
CORPORATE SOURCE: INST NACL MICROBIOL CARLES G MALBRAN,DIV INMUNOL APLICADA,AVE VELEZ SARSFIELD 563/RA-1281 BUENOS AIRES//ARGENTINA/ (Reprint); HOSP PEDRO ELIZALDE/BUENOS AIRES//ARGENTINA/; GOTHENBURG UNIV,DEPT MED MICROBIOL/S-41124 GOTHENBURG//SWEDEN/
PUBLICATION: MEDICINA-BUENOS AIRES, 1992, V52, N2, P103-108
GENUINE ARTICLE#: JD611
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: The incidence of **enterotoxigenic** Escherichia **coli** (**ETEC**) has been studied in 85 children with acute diarrhea in patients in the Hospital de Ninos Pedro de Elizalde, Buenos Aires, and in 38 healthy children. All of them were up to four years old and none had received antibiotic treatment within 7 days before sampling. **ETEC** was recovered in 9 out of 85 (10.6%) children with diarrhea. From these positive cases, 6 were associated with **heat-stable** (**ST**), 1 with **heat-labile** (**LT**) and 2 with both **LT** and **ST enterotoxins**. Only one case (2.6%) of **LT**-producing **ETEC** was detected in the control group. In 5 out of 9 **ETEC** diarrhea cases (55.5%) the isolated strains expressed human colonization factor antigens (CFA); four of them were CFA/I and one CFA/II. The characteristics of the CFA, biotype, serotype and antibiotic sensitivity pattern were studied in 23 E. coli isolates from 10 **ETEC** positive children. Of the 12 **ST** only strains, 5 (41.7%) expressed CFA/I and 2 (16.7%) CFA/II (**CS2** + **CS3**). One out of 2 **LT/ST** strains expressed **CFA/I**. CFAs were not detected in the **ETEC-LT** nor in the **toxin** negative E coli strains. From the **ETEC** isolated, 82.4% were resistant to 4 or more antibiotics, whereas only 50% of simultaneously isolated **toxin**-negative E. coli

presented this sensitivity pattern. The different **ETEC** strains belonged to several different serotypes, some of them rarely observed in other countries. None of these serotypes correlated either with the **toxin** profile or with the sugar fermentation pattern. Interestingly, in three cases, **ETEC** strains with differing serotype but with the same **toxin** profile were detected.

7/3,AB/22 (Item 22 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03052399 References: 43
TITLE: COLONIZATION FACTORS OF **ENTEROTOXIGENIC** ESCHERICHIA-**COLI** ISOLATED FROM CHILDREN WITH DIARRHEA IN ARGENTINA
AUTHOR(S): BINSZTEIN N; JOUVE MJ; VIBOUD GI; MORAL LL; RIVAS M; ORSKOV I; AHREN C; SVENNERHOLM AM
CORPORATE SOURCE: INST NACL MICROBIOL CARLOS G MALBRAN,VELEZ SARSFIELD 563/RA-1281 BUENOS AIRES//ARGENTINA/ (Reprint); STATENS SERUMINST,INT ESCHERICHIA & KLEBSIELLA CTR/DK-2300 COPENHAGEN//DENMARK/; GOTHENBURG UNIV,DEPT MED MICROBIOL & IMMUNOL/S-41346 GOTHENBURG//SWEDEN/
PUBLICATION: JOURNAL OF CLINICAL MICROBIOLOGY, 1991, V29, N9 (SEP), P 1893-1898
GENUINE ARTICLE#: GB716
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: A prospective study was performed to evaluate the presence of colonization factor antigens (CFAs) in **enterotoxigenic** Escherichia **coli** (**ETEC**) strains isolated from 1,211 children with diarrhea in Argentina. One hundred nine **ETEC** strains that were isolated from seven different laboratories in various regions of the country were tested for CFAs by using monoclonal antibodies against CFA/I and the E. coli surface antigens **CS1**, **CS2**, and **CS3** of **CFA/II** and **CS4** and **CS5** of **CFA/IV**; a polyclonal antiserum against **CS6** was used. The CFAs searched for were found in 52% of the **ETEC** strains: 23% of the strains carried **CFA/I**, 17% carried **CFA/IV**, and 12% carried **CFA/II**. All of the **CFA/I** strains produced **heat-stable** enterotoxin, and several of them were of the prevalent serotypes O153:H45 and O78:H12. Among the 19 strains expressing **CFA/IV**, 16 expressed **CS5** and **CS6** and produced the **heat-stable** enterotoxin and most were of serotype O128:H21; the remaining 3 strains produced **CS6** only. No **ETEC** strains expressing **CS4** were found. Most (11 of 13) of the **CFA/II**-carrying **ETEC** strains expressed **CS1** and **CS3**, and 10 of them were of the O6:K15:H16 serotype and produced both **heat-labile** and **heat-stable** toxins. As many as 24 of the 109 CFA-negative **ETEC** strains gave mannose-resistent hemagglutination with erythrocytes from different species; 4 strains had high surface hydrophobicity, suggesting the presence of additional, as yet undefined, colonization factors in up to 25% of the **ETEC** isolates.

7/3,AB/23 (Item 23 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03045837 References: 39
TITLE: POSITIVE REGULATION OF COLONIZATION FACTOR ANTIGEN-I (CFA/I) PRODUCTION BY **ENTEROTOXIGENIC** ESCHERICHIA-**COLI** PRODUCING THE COLONIZATION FACTORS **CS5**, **CS6**, CS7, CS17, PCFO9, PCFO159-H4 AND PCFO166
AUTHOR(S): HIBBERD ML; MCCONNELL MM (Reprint); WILLSHAW GA; SMITH HR; ROWE B
CORPORATE SOURCE: CENT PUBL HLTH LAB,DIV ENTER PATHOGENS,61 COLINDALE AVE/LONDON NW9 5HT//ENGLAND/ (Reprint); CENT PUBL HLTH LAB,DIV ENTER PATHOGENS,61 COLINDALE AVE/LONDON NW9 5HT//ENGLAND/
PUBLICATION: JOURNAL OF GENERAL MICROBIOLOGY, 1991, V137, AUG (AUG), P 1963-1970
GENUINE ARTICLE#: GB638
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: **Enterotoxigenic** Escherichia **coli** (**ETEC**) strains of nineteen serogroups which produced colonization factors (coli-surface-associated antigens CS5, CS6, CS7 and CS17, colonization factor antigen CFA/III and putative colonization factors PCFO159:H4, PCFO166 and PCFO9) were tested for hybridization with a DNA probe containing the cfaD sequence that regulates expression of **CFA/I**. Strong colony hybridization, similar to that with the **CFA/I**-positive control strain H10407, occurred with **ETEC** strains of serogroups O27, O159 and O169 which produced **CS6** antigen, and with all the strains which produced PCFO166 fimbriae. Weak colony hybridization, compared to the control strain, was found with **ETEC** producing **CS5** fimbriae with **CS6** antigen, CFA/III fimbriae with **CS6** antigen, CS7 fimbriae or PCFO159:H4 fimbriae. **CS6**-antigen-positive strains of serogroups O79, O89 and O148 and all the CS17-antigen-positive and PCFO9-fimbriae-positive strains were negative in colony hybridization tests with the cfaD probe. Plasmid DNA of nine **ETEC** strains and their colonization-factor-negative derivatives was tested for hybridization with the cfaD probe and with **ST** and **LT** oligonucleotide probes. The sequences that hybridized with the cfaD probe were on the plasmids which coded for **enterotoxin** production. Fifteen strains were transformed with NTP513, a recombinant plasmid which contains the **CFA/I** region **1** fimbrial subunit operon but lacks a functional cfaD sequence, in order to determine whether DNA in any of these strains could substitute for the cfaD sequence in the regulation of production of **CFA/I** fimbriae. Transformants of five strains which produced the colonization factors **CS6**, PCFO166, **CS5** + **CS6**, CS7 and PCFO9, and of one strain which was a colonization-factor-negative derivative of the **CS5,CS6**-producing strain E17018, gave good production of **CFA/I** fimbriae comparable to the **CFA/I**-positive control strain H10407. Transformants of two strains, producing PCFO159 fimbriae and CS17 antigen, respectively, gave weak **CFA/I** production. Transformants of one strain producing **CS6** antigen and of six colonization-factor-negative derivatives did not produce **CFA/I** fimbriae. These results showed that plasmids in seven of eight types of colonization-factor-positive strains contained gene sequences which could substitute functionally for the cfaD sequence. Only two of these strains had gene sequences that hybridized strongly with the cfaD probe.

7/3,AB/24 (Item 24 from file: 440)

DIALOG(R)File 440:Current Contents Search(R)

02709056 References: 44
TITLE: NEW ADHESIVE FACTOR (ANTIGEN-8786) ON A HUMAN **ENTEROTOXIGENIC** ESCHERICHIA-**COLI** O117-H4 STRAIN ISOLATED IN AFRICA
AUTHOR(S): AUBEL D; DARFEUILLEMICHAUD A (Reprint); JOLY B
CORPORATE SOURCE: FAC PHARM CLERMONT FERRAND,SERV BACTERIOL VIROL/F-63001 CLERMONT FERRAND//FRANCE/ (Reprint); FAC PHARM CLERMONT FERRAND,SERV BACTERIOL VIROL/F-63001 CLERMONT FERRAND//FRANCE/
PUBLICATION: INFECTION AND IMMUNITY, 1991, V59, N4 (APR), P1290-1299
GENUINE ARTICLE#: FD915
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: An **enterotoxigenic** Escherichia **coli** strain, E. coli 8786, of serotype O117:H4 produced only **heat-stable** enterotoxin and gave mannose-resistant hemagglutination with human and bovine erythrocytes. The strain adhered to the brush border of human enterocytes and to enterocytelike cell line Caco-2. Adhesion inhibition assays using Caco-2 cells with different adhesive factor extracts showed that the adhesive factor of E. coli 8786 is different from colonization factor antigen I (CFA/I), CFA/II, CFA/III of Darfeuille et al. (A. Darfeuille, B. Lafeuille, B. Joly, and R. Cluzel, Ann. Microbiol. Inst. Pasteur 134A:53-64, 1983), **CS6**, and antigen 2230. A bacterial surface protein, designated antigen 8786, with a molecular mass of 16,300 Da was responsible for the adhesion to intestinal cells. It was immunologically different from previously described adhesive factors as determined by immunoblotting. Antigen 8786 was detected on the bacterial cell surface and appeared to be nonfimbrial. NH2-terminal analysis of antigen 8786 showed no homology with the previously described adhesive factors. Nevertheless, antigen 8786 is closely related to the NH2-terminal sequence of Salmonella enteritidis fimbrin. A hybridization experiment using a synthetic oligonucleotide probe based on the NH2-terminal amino acid sequence of antigen 8786 revealed that the coding region was located on a 70-MDa plasmid.

7/3,AB/25 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00616188
DELETION MUTANTS AS VACCINES FOR CHOLERA
DELETIONSMUTANTEN ALS IMPFSTOFFE GEGEN CHOLERA
MUTANTS DE DELETION UTILISES EN TANT QUE VACCINS CONTRE LE CHOLERA
PATENT ASSIGNEE:
PRESIDENT AND FELLOWS OF HARVARD COLLEGE, (227955), 17 Quincy Street, Cambridge Massachusetts 02138, (US), (Proprietor designated states: all)
VIRUS RESEARCH INSTITUTE, (1754330), 61 Moulton Street, Cambridge, MA 02138, (US), (Proprietor designated states: all)
INVENTOR:
MEKALANOS, John J., 78 Fresh Pond Lane, Cambridge, MA 02138, (US)
BEATTIE, David, 10 Neponset Court, Boston, MA 02131, (US)
KILLEEN, Kevin, 1112 Brook Road, Milton, MA 02186, (US)
LU, Yichen, 15 South Woodside Avenue, Wellesley, MA 02181, (US)

LEGAL REPRESENTATIVE:
Deans, Michael John Percy et al (30021), Lloyd Wise, Tregear & Co., Commonwealth House, 1-19 New Oxford Street, London WC1A 1LW, (GB)
PATENT (CC, No, Kind, Date): EP 672116 A1 950920 (Basic)
EP 672116 A1 960612
EP 672116 B1 030604
WO 94001533 940120
APPLICATION (CC, No, Date): EP 93916907 930701; WO 93US6270 930701
PRIORITY (CC, No, Date): US 909382 920706
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/01; C12N-001/21; A61K-039/106
NOTE:
No A-document published by EPO
Figure number on first page: NONE
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200323	875
CLAIMS B	(German)	200323	781
CLAIMS B	(French)	200323	947
SPEC B	(English)	200323	12230
Total word count - document A			0
Total word count - document B			14833
Total word count - documents A + B			14833

7/3,AB/26 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00557311
PREPARATION AND USE OF FORMALIN-KILLED COLONIZATION-FACTOR-ANTIGEN (CFA)-EXPRESSING E. COLI ORGANISMS FOR VACCINATION AGAINST ENTERIC INFECTION/DIARRHEA CAUSED
DARSTELLUNG UND VERWENDUNG VON MIT FORMALIN ABGETOTETEN E. COLI BAKTERIEN, DIE DAS KOLONIE-FAKTOR-ANTIGEN (CFA) EXPREMIEREN ZUR IMPFUNG GEGEN DAS DIE DARMINFEKT
PREPARATION ET UTILISATION D'ORGANISMES DE E. COLI TUES DANS LE FORMOL ET EXPRIMANT UN ANTIGENE DE FACTEUR DE COLONISATION (CFA) DANS LE BUT D'UNE VACCINATION C
PATENT ASSIGNEE:
Holmgren, Jan, (1145760), Korvettgatan 1D, S-421 74 Vastra Frolunda, (SE), (applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;MC;NL;SE)
SVENNERHOLM, Ann-Mari, (1553120), Korvettgatan 1D, S-421 74 Vastra Frolunda, (SE), (applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;MC;NL;SE)
INVENTOR:
Holmgren, Jan, Korvettgatan 1D, S-421 74 Vastra Frolunda, (SE)
SVENNERHOLM, Ann-Mari, Korvettgatan 1D, S-421 74 Vastra Frolunda, (SE)
LEGAL REPRESENTATIVE:
Nilsson, Brita Linnea et al (23742), OSCAR GRAHN PATENTBYRA AB, Box 19540, 104 32 Stockholm, (SE)
PATENT (CC, No, Kind, Date): EP 573527 A1 931215 (Basic)
EP 573527 B1 980909

WO 9214487 920903
APPLICATION (CC, No, Date): EP 92906078 920225; WO 92SE110 920225
PRIORITY (CC, No, Date): SE 91556 910226
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; MC; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/108;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9837	281
CLAIMS B	(German)	9837	264
CLAIMS B	(French)	9837	321
SPEC B	(English)	9837	5891
Total word count - document A			0
Total word count - document B			6757
Total word count - documents A + B			6757

7/3,AB/27 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0312509 DBR Accession No.: 2003-13649 PATENT
New Escherichia coli cell useful in manufacturing a medicament for vaccination against diarrhea, expresses **colonization factor antigen CFA/I, CS5** and/or **CS6** from a native plasmid, but does not express **heat stable** toxin - plasmid-mediated chloramphenicol-acetyltransferase reporter gene transfer and expression in Escherichia coli for recombinant protein production for use as a recombinant vaccine
AUTHOR: TURNER A K; GREENWOOD J; STEPHENS J C; BEAVIS J C; DARSLEY M J
PATENT ASSIGNEE: ACAMBIS RES LTD 2003
PATENT NUMBER: WO 200322307 PATENT DATE: 20030320 WPI ACCESSION NO.: 2003-301010 (200329)
PRIORITY APPLIC. NO.: GB 200121998 APPLIC. DATE: 20010911
NATIONAL APPLIC. NO.: WO 2002GB4164 APPLIC. DATE: 20020911
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - A bacterial cell which expresses **colonization factor antigen CFA/I, CS5** and/or **CS6** from a native plasmid, but does not express **heat stable toxin (ST)**, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) a native **enterotoxigenic** Escherichia **coli** plasmid in which the gene encoding **ST toxin** is deleted or inactivated and which encodes **colonization factor antigen CFA/I, CS5** and/or **CS6**; (2) a vaccine against diarrhea, comprising the cell cited above and a carrier or diluent; (3) vaccinating a mammal against diarrhea, comprising administering to the mammal the above cell or vaccine; (4) a suicide vector which is less than 5 kb in size and comprises the sacB region which codes for a product that is toxic to bacteria when grown on sucrose, in which region the IS 1 insertion sequence is deleted or inactivated; and (5) producing a bacterial cell in which a target gene is deleted, inactivated or replaced, comprising transferring the above vector into

a bacterial cell containing the target gene and selecting for a cell in which the target gene has been deleted, inactivated or replaced. BIOTECHNOLOGY - Preferred Cell: The bacterial cell is an E. coli cell that is deposited with the European Collection of Cell Cultures (ECACC) under accession number 01090303, 01090304, 01090305, 01090306, 02082964, 02082965, 02082966, 02082967 or 02082968. The plasmid is an **enterotoxigenic** E. **coli** plasmid in which the **ST** gene is inactivated or deleted. The plasmid contains a deletion of all or part of the **ST** gene, and also an element that enhances its stability. The cell does not also express **heat labile toxin** (**LT**), EAST1 or an antibiotic resistance gene. It is obtainable by a method comprising deletion of all or part of the **ST** gene with a suicide vector, or site-directed deletion or inactivation of the **LT** gene, the EAST1 gene and/or one or more antibiotic resistance genes. The element cited above is a **toxin-antitoxin** element or a recombinase recognition element. The stability element is parDE or crs. The cell is further attenuated by a site-directed deletion o r inactivation of aroA, aroC, aroD, aroE, pur, htrA, ompC, ompF, ompR, cya, crp, phoP, surA, rfaY, dksA, hupA, sipC and clpB. It expresses a heterologous antigen, particularly an E. coli colonization factor antigen (CFA). The heterologous antigen is a non-toxic component or form of **LT**, particularly the B subunit. Preferred Vaccine: The vaccine further comprises a cell that expresses **colonization factor antigen CFA/II**, **CS1**, **CS2**, **CS3** or **CS4**. The cell that expresses **CFA/I** is deposited with ECACC under accession number 01090303 or 02082967; the cell expressing **CS5** and **CS6** is deposited with ECACC under accession number 01090305 or 02082968; the cell that expresses **CS4** and **CS6** is deposited with ECACC under accession number 01090306 or 02082966; the cell expressing **CS2** and **CS3** is deposited with ECACC under accession number 01090304 or 02082964; and the cell expressing **CS1** and **CS3** is deposited with ECACC under accession number 01090302 or 02082965. Preferred Vector: The vector further comprises a transfer origin that directs conjugative transfer of the vector from one bacterial strain to another, an origin of replication, a selectable marker, and a cloning site comprising at least one restriction enzyme site unique in the vector. The transfer origin is mobRP4. The origin of replication is oriR6K that requires the pir gene for replication. The selectable marker is the cat gene that codes for chloramphenicol acetyltransferase and confers resistance to chloramphenicol. The vector is about 3 kb in size. It comprises a sequence of a target gene or a wild type or inactivated **ST** gene or E. coli **toxin** gene in the cloning site. Preferred Method: Producing a bacterial cell in which a target gene is deleted, inactivated or replaced, comprises carrying out polymerase chain reaction (PCR) to select for a cell in which the vector has correctly targeted to the target gene, where one of the primers used in the PCR hybridizes to vector sequence adjacent to the cloning site and the other hybridizes to a site in the cellular DNA adjacent to the target gene, and where a positive PCR indicates that the vector has targeted to the target gene. It comprises selecting for a cell from which the vector has been excised by growing the cell in a medium supplemented with sucrose from which NaCl is absent. ACTIVITY - Antibacterial; Antidiarrheal. No biological data is given.MECHANISM OF ACTION - Vaccine. USE - The cell is useful in manufacturing a medicament for vaccination against diarrhea (claimed). ADMINISTRATION -

A dosage of about 107 to 1011 bacteria per dose may be convenient for a 70 kg adult human. Administration is by oral means. EXAMPLE - No relevant example given. (51 pages)

7/3,AB/28 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0312276 DBR Accession Number: 2003-13416 PATENT
New bacterial cell expressing three or more coli surface antigens, useful for manufacturing a medicament, i.e. a vaccine, for vaccination against diarrhea - vector-mediated gene transfer and expression in Escherichia coli for recombinant protein production for use as a recombinant vaccine
AUTHOR: TURNER A K; GREENWOOD J; STEPHENS J C; BEAVIS J C; DARSLEY M J
PATENT ASSIGNEE: ACAMBIS RES LTD 2003
PATENT NUMBER: WO 200322306 PATENT DATE: 20030320 WPI ACCESSION NO.: 2003-301009 (200329)
PRIORITY APPLIC. NO.: GB 200121998 APPLIC. DATE: 20010911
NATIONAL APPLIC. NO.: WO 2002GB4123 APPLIC. DATE: 20020911
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - A bacterial cell expressing three or more coli surface antigens, and deposited under accession number 02082969 at the ECACC, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) a vaccine against diarrhea comprising: (a) the bacterial cell cited above and a pharmaceutical carrier or diluent; or (b) bacterial cells which together express all of **colonization factor antigen** (**CFA**)/**I**, coli surface (**CS**)**1**, **CS2**, **CS3**, **CS4**, **CS5** and **CS6**, where the vaccine comprises fewer than five bacterial strains; and (b) vaccinating a mammal against diarrhea comprising administering to the mammal the bacterial cell cited above or the vaccine of (1). BIOTECHNOLOGY - Preparation (claimed): Making the cell comprises introducing a polynucleotide encoding a heterologous CS antigen into a bacterial cell. Preferred Cell: The cell is an Escherichia **coli** cell, preferably an **enterotoxigenic** E. **coli** (**ETEC**) cell. The coli surface (CS) antigens are **ETEC** CS antigens, such as **CS1**, **CS2**, **CS3**, **CS4**, **CS5** or **CS6**. The cell expresses **CS1**, **CS2** and **CS3**, **CS4**, **CS5** and **CS6**, or **CS1**, **CS3** and **CS4**. The cell is attenuated by deletion or inactivation of a gene, such as aroA, aroC, aroD, aroE, pur, htrA, ompC, ompF, ompR, cya, crp, proP, phoQ, surA, rfaY, dksA, hupA, invE, or clpB, preferably at least one aro gene and at least one omp gene, at least one aro gene and the htrA gene, or aroC, ompF and ompC. The cell does not express one or more of **heat stable toxin** (**ST**), **heat labile toxin** (**LT**) or EAST 1, or an antibiotic resistance gene. The cell further expresses a heterologous antigen in addition to the CS antigens. The heterologous antigen is an E. coli antigen, or a non-toxic component or form of **LT** , preferably the B subunit. The cell is obtained by a method comprising: (a) deletion of all or a part of the **ST** gene with a suicide vector; (b) site directed deletion or inactivation of the **LT** gene and/or the EAST 1 gene; or (c) introduction of a polynucleotide encoding a heterologous CS antigen into a bacterial

cell. The polynucleotide comprises the operon of the heterologous CS antigen. The method comprises introducing a polynucleotide encoding a regulatory protein into the cell. The heterologous CS antigen coding sequence is carried on a stable plasmid in the cell, or inserted in the bacterial chromosome of the cell. Preferred Method: Making the bacterial cell comprises: (a) introducing a polynucleotide encoding **ETEC CS4** antigen into a **CS5/CS6 ETEC** cell; (b) introducing a polynucleotide encoding **ETEC CS1** antigen into a **CS2/CS3 ETEC** cell; (c) introducing a polynucleotide encoding **ETEC CS5** antigen into a **CS4/CS6 ETEC** cell; or (d) introducing a polynucleotide encoding **ETEC CS4** antigen into a **CS1/CS3 ETEC** cell.
Preferred Vaccine: The vaccine comprises three bacterial strains. The vaccine also comprises: (a) a strain that expresses **CS1, CS2** and **CS3**; (b) a strain that expresses **CS4, CS5** and **CS6**; and (c) a strain that expresses **colonization factor antigen (CFA)/I** .
ACTIVITY - Antidiarrheic; Antibacterial. No biological data given. MECHANISM OF ACTION - Vaccine. USE - The bacterial cell is useful for manufacturing a medicament, i.e. a vaccine, for vaccination against diarrhea (claimed). The vaccine is also useful for targeting bacterial infection. ADMINISTRATION - Dosage is about 107-1011, preferably 108-1010, bacteria per dose for a 70 kg adult human host. Administration is preferably oral. EXAMPLE - No relevant example given. (115 pages)

7/3,AB/29 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0095164 DBR Accession Number: 89-13155
Molecular cloning and characterization of the **CS5** and **CFA IV** fimbrial antigens from **enterotoxigenic** Escherichia **coli** (**ETEC**) - for use in vaccine development (conference abstract)
AUTHOR: Neal B L; Elliot T R; Heuzenroeder M W; Manning P A
CORPORATE SOURCE: Department of Microbiology and Immunology, The University of Adelaide, Adelaide, South Australia, Australia.
JOURNAL: Aust.Microbiol. (9, 2, ASM 13 Meet., 223) 1988
CODEN: 9999Y
LANGUAGE: English
ABSTRACT: **Enterotoxigenic** Escherichia **coli** (**ETEC**) cells have 2 major virulence factors: **toxins**, which can be either **heat-labile** (**LT**) or **heat-stable** (**ST**), as well as colonization factor antigens (CFA) also called fimbriae. These factors allow stable colonization of the gut. The detection of 2 fimbrial types is described: CS5 and **CFA/IV** . Their molecular cloning, comparative physical properties, NH2-terminal amino acid sequences and genetic organization are also described. The cloning and characterization of these factors may be of use in producing vaccines against diarrhea caused by **ETEC**. (0 ref)

Set	Items	Description
S8	213	AU=(CARLIN, N? OR CARLIN N?)
S9	20	AU=(ASKELOF, P? OR ASKELOF P?)

-Author (s)

Searcher : Shears 571-272-2528

S10 14 AU=(BJARE, U? OR BJARE U?)
S11 1 S8 AND S9 AND S10
S12 3 S8 AND (S9 OR S10)
S13 1 S9 AND S10
S14 0 (S8 OR S9 OR S10) AND S5
S15 3 (S11 OR S12 OR S13) NOT S6
S16 3 RD (unique items)
>>>No matching display code(s) found in file(s): 65, 113

16/3,AB/1 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
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01183250
ORAL VACCINE AGAINST DIARRHEA
ORALER IMPFSTOFF GEGEN DIARRHOE
VACCIN ORAL CONTRE LA DIARRHEE
PATENT ASSIGNEE:
SBL VACCIN AB, (2076680), Lundagatan 2, 105 21 Stockholm, (SE),
(Applicant designated States: all)
INVENTOR:
CARLIN, Nils, Stallknektsgrand 14, S-165 57 Hasselby, (SE)
ASKELOF, Per, Aspvagen 1A, S-191 41 Sollentuna, (SE)
BJARE, Ulf, Noth rsvagen 80, S-757 57 Uppsala, (SE
LEGAL REPRESENTATIVE:
Woods, Geoffrey Corlett et al (48721), J.A. KEMP & CO. Gray's Inn 14
South Square, London WC1R 5JJ, (GB)
PATENT (CC, No, Kind, Date): EP 1140159 A1 011010 (Basic)
WO 200037106 000629
APPLICATION (CC, No, Date): EP 99964847 991209; WO 99SE2306 991209
PRIORITY (CC, No, Date): SE 984415 981218
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI;
LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-039/108
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

16/3,AB/2 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
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00748052
A METHOD OF CULTIVATING BACTERIA PRODUCING PROTEINS THAT ARE EXPRESSED IN A TEMPERATURE REGULATED MANNER
EIN VERFAHREN ZUR KULTIVIERUNG VON BAKTERIEN, DIE PROTEINE HERSTELLEN, DEREN EXPRESSION DURCH TEMPERATUR REGULIERT WIRD
PROCEDE DE CULTURE DE BACTERIES PRODUISANT DES PROTEINES A EXPRESSION REGULEE PAR LA TEMPERATURE
PATENT ASSIGNEE:
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designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
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Woods, Geoffrey Corlett et al (48721), J.A. KEMP & CO. Gray's Inn 14 South Square, London WC1R 5JJ, (GB)
PATENT (CC, No, Kind, Date): EP 759981 A1 970305 (Basic)
WO 9533825 951214
APPLICATION (CC, No, Date): EP 95921214 950601; WO 95SE628 950601
PRIORITY (CC, No, Date): SE 941921 940603
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/00; C12N-001/21; C12N-015/70;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

16/3,AB/3 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0192481 DBR Accession No.: 96-02674 PATENT
Temperature regulated cultivation of bacteria expressing surface antigens - temp.-regulated plasmid-mediated Escherichia coli surface antigen expression and fermentation for large-scale recombinant vaccine production
AUTHOR: **Askelof P; Carlin N;** Nilson B; Paulsson A
CORPORATE SOURCE: Stockholm, Sweden.
PATENT ASSIGNEE: SBL-Vaccin 1995
PATENT NUMBER: WO 9533825 PATENT DATE: 951214 WPI ACCESSION NO.: 96-058138 (9606)
PRIORITY APPLIC. NO.: SE 941921 APPLIC. DATE: 940603
NATIONAL APPLIC. NO.: WO 95SE628 APPLIC. DATE: 950601
LANGUAGE: English
ABSTRACT: A method is claimed for the cultivation of bacteria containing plasmids consisting of genes encoding surface or membrane-bound antigens or other proteins which are expressed in a temperature-regulated manner for the production of desired bacterial products, involving: (a) culture of the bacteria in a medium at a temperature such that the bacteria retain their plasmids, but no expression occurs (preferably at room temperature, specifically at approximately 20 deg); (b) further culture of the inoculum in a medium at a temperature at which expression occurs (preferably at the body temperature of a mammal, specifically at 34-39 deg); (c) harvesting of the bacteria prior to them losing the plasmids; and (d) isolation of the desired product. Preferably the bacterium is Escherichia coli expressing at least one type of colonization factor antigen selected from CFA/I, CS1, CS2, CS3, CS4, CS5 and CS6. This method is used to produce commercial quantities of E. coli with intact colonization factor antigens and sub-components in large-scale industrial fermentors. The bacteria can be inactivated and used to prepare recombinant vaccines against E. coli. (10pp)
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27apr04 11:44:08 User219783 Session D2012.4

Devi, S.
09/868243

(FILE 'HCAPLUS' ENTERED AT 11:26:36 ON 27 APR 2004)
L12 3020 SEA FILE=HCAPLUS ABB=ON PLU=ON (ENTEROTOX? OR ENTERO TOX?)(3A)COLI OR ETEC(S)COLI
L13 388 SEA FILE=HCAPLUS ABB=ON PLU=ON CFA1 OR CFA2 OR CFA4 OR CFAI OR CFAII OR CFAIV OR (CFA OR COLON? FACTOR ANTIGEN)(2W)(1 OR 2 OR 4 OR I OR II OR IV)
L14 91 SEA FILE=HCAPLUS ABB=ON PLU=ON L13(S)(CS1 OR CS2 OR CS3 OR CS4 OR CS5 OR CS6 OR (CS OR SURFACE ANTIGEN)(W)(1 OR 2 OR 3 OR 4 OR 5 OR 6) OR SBL101 OR SBL106 OR SBL107 OR SBL104 OR SBL105 OR SBL(W)(101 OR 106 OR 107 OR 104 OR 105))
L15 82 SEA FILE=HCAPLUS ABB=ON PLU=ON L12 AND L14
L16 20 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 AND ((LT OR ST)(S)(ENTEROTOXIN OR TOXIN) OR HEAT(W)(LABILE OR STABLE) OR CTB OR CHOLERA(3A)B)

-key terms

L16 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 13 May 2003
ACCESSION NUMBER: 2003:361598 HCAPLUS
DOCUMENT NUMBER: 139:163321
TITLE: Safety and immunogenicity of an oral, inactivated **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B** subunit vaccine in Bangladeshi children 18-36 months of age
AUTHOR(S): Qadri, Firdausi; Ahmed, Tanvir; Ahmed, Firoz; Bradley Sack, R.; Sack, David A.; Svennerholm, Ann-Mari
CORPORATE SOURCE: PTE study group, Laboratory Sciences Division, International Centre for Diarrhoeal Disease Research, Dhaka, 1000, Bangladesh
SOURCE: Vaccine (2003), 21(19-20), 2394-2403
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A phase II safety and immunogenicity study of an oral-formalin inactivated **enterotoxigenic** Escherichia **coli** (**ETEC**) vaccine containing six colonization factors (**CFA/I, CS1, CS2, CS3, CS4, CS5**) and 1 mg of recombinant **cholera** toxin **B** subunit (the CF-BS-**ETEC** vaccine) was carried out in an urban slum of Dhaka city in Bangladesh. The study was carried out in a double blinded, placebo controlled design in 158 children, 18-36 mo of age. Children were given two doses of the CF-BS-**ETEC** vaccine or the placebo which consisted of E. **coli** K12. The vaccine was well tolerated. The immune response was studied in 60 children (30 each in the placebo and vaccine group). Significant vaccine specific IgA antibody-secreting cell (ASC) responses were seen 7 days after ingestion of the first and second dose of the vaccine. The responses to **CFA/I, CS2, CS4** and rCTB were elevated in the vaccines in comparison to the pre-immune values and in comparison to those seen in the placebo recipients (to <0.001). Vaccines but not placebo recipients also showed significantly increased IgM ASC responses to all three CF antigens that were

tested (to <0.001) and IgG-ASCs to rCTB. Peak ASC levels were reached after one dose of the vaccine with no further increase or decrease after the second dose. The vaccine recipients also responded with IgA plasma antibodies to **CFA/I, CS1, CS2, CS4** and rCTB after one or two doses of the vaccine (to <0.001). Subjects in the placebo group failed to mount responses to any of the antigens. The vaccine also induced responses in mucosal IgA antibodies in feces to **CFA /I, CS2** and rCTB (61, 88 and 69% responder frequency, resp.) and the magnitude of the response was elevated in comparison to the pre-immune levels (to <0.001) and to the levels of the control group (to <0.001). This study thus shows that the CF-BS-ETEC vaccine is well tolerated in children, 18-36 mo of age and gives rise to significant systemic and mucosal IgA antibody responses.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 23 Apr 2003
ACCESSION NUMBER: 2003:311581 HCAPLUS
DOCUMENT NUMBER: 139:163296
TITLE: Mucosal immunization of BALB/c mice using **enterotoxigenic** Escherichia **coli** colonization factors **CFA/I** and **CS6** administered with and without a mutant **heat-labile** enterotoxin
AUTHOR(S): Byrd, Wyatt; Cassels, Frederick J.
CORPORATE SOURCE: Department of Enteric Infections, Walter Reed Army Institute of Research, Silver Spring, MD, 20910-7500, USA
SOURCE: Vaccine (2003), 21(17-18), 1884-1893
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mice (BALB/c) were intranasally (IN) and intragastrically (IG) administered the ETEC colonization factors (CF), **CFA/ I** and **CS6**, with and without the R192G mutant **heat-labile** enterotoxin (mLT), and immunogenicity and efficacy measured. The IN administration of CFA/I to mice induced strong serum and fecal IgG and IgA responses. The IG administration of CFA/I to mice induced serum IgG and fecal IgA responses, but only when mLT was co-administered with CFA/I were serum IgA titers detected. The IN administration of CS6 to mice induced serum IgG antibodies, and mLT, when co-administered with CS6, enhanced the serum IgG response. Only when the mLT was co-administered with CS6, were serum and fecal IgA responses detected. The IG administration of CS6 plus mLT induced serum IgG and fecal IgA responses. Partial protection against lethal challenge with ETEC strain H10407 was seen in the mice IN administered the CFA/I plus mLT, and H10407 was cleared from the lungs of CFA/I plus mLT-immunized mice at a significantly greater rate than from the control mice. **CFA/I** and

CS6 administered IN and IG induced mixed Th1/Th2 immune responses with the Th2 type being predominant as evidenced by IgG1 > IgG2a. The administration of colonization factors to mice, particularly by the IN route, potentially serves as a useful way to measure the serum and mucosal immune responses to these antigens prior to their use in volunteers.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 25 Feb 2003
ACCESSION NUMBER: 2003:142409 HCAPLUS
DOCUMENT NUMBER: 138:379861
TITLE: Development and evaluation of genotypic assays for the detection and characterization of **enterotoxigenic** Escherichia **coli**
AUTHOR(S): Steinsland, Hans; Valentiner-Branth, Palle; Grewal, Harleen M. S.; Gaastra, Wim; Molbak, Kare; Sommerfelt, Halvor
CORPORATE SOURCE: Centre for International Health, University of Bergen, Norway
SOURCE: Diagnostic Microbiology and Infectious Disease (2003), 45(2), 97-105
CODEN: DMIDDZ; ISSN: 0732-8893
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We developed and evaluated a method to genotypically identify **enterotoxigenic** Escherichia **coli** (**ETEC**) and to characterize these organisms with respect to 18 of 21 known colonization factors (CFs). The method, which is based on polynucleotide DNA-DNA colony hybridization, includes a pooled **toxin** probe assay to identify ETEC, and individual probe assays to detect the **enterotoxins** STp, STh, and **LT**, and the CFs **CFA/I**, **CS1**-CS8, CS12-CS15, CS17-CS19, CS21, and CS22. We evaluated the pooled toxin probe assay during a cohort study of childhood diarrhea, and the individual probe assays against 33 reference strains and 92 clin. ETEC isolates. There was close to a complete agreement between the pooled toxin probe assay and the individual toxin probe assays, and between the individual CF probe assays and the corresponding phenotypic assays.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 14 Jan 2003
ACCESSION NUMBER: 2003:31682 HCAPLUS
DOCUMENT NUMBER: 138:270025
TITLE: Immune responses elicited against multiple **enterotoxigenic** Escherichia **coli** fimbriae and mutant LT expressed in attenuated Shigella vaccine strains
AUTHOR(S): Barry, Eileen M.; Altboum, Zeev; Losonsky,

Genevieve; Levine, Myron M.
CORPORATE SOURCE: Center for Vaccine Development, University of Maryland, Baltimore, MD, 21201, USA
SOURCE: Vaccine (2003), 21(5-6), 333-340
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Shigella and **enterotoxigenic** E. **coli** (**ETEC**) continue to be important causes of diarrheal disease in infants and young children in developing countries and are major etiol. agents of traveler's diarrhea. Since attenuated strains of Shigella have been developed as live oral vaccines against shigellosis, the authors have adapted these attenuated Shigella strains to serve as carriers of ETEC antigens, thereby constituting a hybrid vaccine. Since protective immunity against ETEC is largely directed against fimbrial antigens (of which there are multiple antigenic types), the authors have individually expressed 4 different ETEC fimbriae, including **CFA/I**, **CS2**, **CS3**, and **CS4**, using ΔguaBA attenuated Shigella vaccine strain CVD 1204 as a prototype live vector. Following mucosal (intranasal) immunization of guinea pigs, serum IgG and mucosal IgA responses were elicited against each fimbrial type. An addnl. strain was constructed expressing a detoxified version of the human ETEC variant of **heat labile** toxin (LThK63). Following mucosal immunization of guinea pigs with a mixed inoculum containing 5 Shigella strains each expressing a different ETEC antigen, immune responses were observed against each ETEC antigen plus the Shigella vector.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 09 Jan 2003
ACCESSION NUMBER: 2003:18454 HCAPLUS
DOCUMENT NUMBER: 138:105328
TITLE: Pathogenicity and immune response measured in mice following intranasal challenge with **enterotoxigenic** Escherichia **coli** strains H10407 and B7A
AUTHOR(S): Byrd, Wyatt; Mog, Steven R.; Cassels, Frederick J.
CORPORATE SOURCE: Department of Enteric Infections, Walter Reed Army Institute of Research, Silver Spring, MD, 20910-7500, USA
SOURCE: Infection and Immunity (2003), 71(1), 13-21
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pathogenicity and immunogenicity induced in BALB/c mice by intranasal (i.n.) inoculation of **enterotoxigenic** Escherichia **coli** (**ETEC**) strains H10407 (O78:H11: **CFA/I**:LT+:ST+) and B7A (O148:H28:**CS6**:LT+:ST+) (two **ETEC** strains previously used in human

challenge trials) were studied. The i.n. inoculation of BALB/c mice with large doses of ETEC strains H10407 and B7A caused illness and death. The H10407 strain was found to be consistently more virulent than the B7A strain. Following i.n. challenge with nonlethal doses of H10407 and B7A, the bacteria were cleared from the lungs of the mice at a steady rate over a 2-wk period. Macrophages and neutrophils were observed in the alveoli and bronchioles, and lymphocytes were observed in the septa, around vessels, and in the pleura of the lungs in mice challenged with H10407 and B7A. In mice i.n. challenged with H10407, serum IgG and IgM antibodies were measured at high titers to the CFA/I and O78 lipopolysaccharide (LPS) antigens. In mice i.n. challenged with B7A, low serum IgG antibody titers were detected against CS6, and low serum IgG and IgM antibody titers were detected against O148 LPS. The serum IgG and IgM antibody titers against the **heat-labile** enterotoxin were equivalent in the H10407- and B7A-challenged mice. The CFA/I and O78 LPS antigens gave mixed T-helper cell 1-T-helper cell 2 (Th1-Th2) responses in which the Th2 response was greater than the Th1 response (i.e., stimulated primarily an antibody response). These studies indicate that the i.n. challenge of BALB/c mice with ETEC strains may provide a useful animal model to better understand the immunogenicity and pathogenicity of ETEC and its virulence determinants. This model may also be useful in providing selection criteria for vaccine candidates for use in primate and human trials.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 05 Aug 2002
ACCESSION NUMBER: 2002:580876 HCAPLUS
DOCUMENT NUMBER: 137:166031
TITLE: Prevalence of **enterotoxigenic** Escherichia **coli** strains harboring the longus pilus gene in Brazil
AUTHOR(S): Nishimura, Lucilia S.; Giron, Jorge A.; Nunes, Solange L.; Guth, Beatriz E. C.
CORPORATE SOURCE: Departamento de Microbiologia, Imunologia e Parasitologia, Universidade Federal de Sao Paulo Escola Paulista de Medicina, UNIFESP, Sao Paulo, Brazil
SOURCE: Journal of Clinical Microbiology (2002), 40(7), 2606-2608
CODEN: JCMIDW; ISSN: 0095-1137
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The longus type IV pilus gene (lngA) was highly prevalent (32.8%) among Brazilian **enterotoxigenic** Escherichia **coli** strains producing both **heat-labile** and **heat-stable** enterotoxins and bearing the **CFA/I**, CS1CS3, or **CS6** antigen. Furthermore, lngA was more often found in strains isolated from children with diarrhea than in strains isolated from children without diarrhea.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE

FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L16 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 03 Jul 2002
ACCESSION NUMBER: 2002:500149 HCAPLUS
DOCUMENT NUMBER: 138:51198
TITLE: Simultaneous expression of CS3 colonization factor antigen and **LT**-B/**ST** fusion **enterotoxin** antigen of **enterotoxigenic** Escherichia **coli** by attenuated Salmonella typhimurium
AUTHOR(S): Xu, Bing; Zhang, Zhaoshan; Li, Shuqin; Shu, Dong; Huang, Cuifen
CORPORATE SOURCE: Beijing Institute of Biotechnology, Beijing, 100071, Peop. Rep. China
SOURCE: Yichuan Xuebao (2002), 29(4), 370-376
CODEN: ICHPCG; ISSN: 0379-4172
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The simultaneous expression of CS3 colonization factor antigen and **LT**-B/**ST** fusion **enterotoxin** antigen of **enterotoxigenic** Escherichia **coli** by attenuated Salmonella typhimurium was studied. **LT** and **ST** are the main **enterotoxins** of **enterotoxigenic** Escherichia **coli** (**ETEC**) found in clin. isolates, and **CS3** (the common antigen in the **CFA**/**II** family of fimbrial antigens) is one of the most prevalent antigens of colonization factors. The genetic determinants encoding CS3 and **LT**-B/**ST** fusion **toxin** were manipulated so that these important antigens are expressed simultaneously in attenuated Salmonella typhimurium oral vaccine strain X4072. These antigens produced by X4072 (pXZL88) could be recognized with monospecific CS3, LT or ST antibodies resp. The specific antibodies against CS3, LT and ST could be detected. in the sera of immunized mice via oral route with the live bacteria. Significantly, the antibody to ST was able to neutralize the biol. activity of native ST. This prototype construct may be proved to the useful in investigating the live vector approach to immunoprophylaxis of ETEC diarrhea disease.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 02 May 2001
ACCESSION NUMBER: 2001:309879 HCAPLUS
DOCUMENT NUMBER: 135:91195
TITLE: Induction of systemic antifimbria and antitoxin antibody responses in Egyptian children and adults by an oral, killed **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B** subunit vaccine
AUTHOR(S): Hall, Eric R.; Wierzba, Thomas F.; Ahren,

Christina; Rao, Malla R.; Bassily, Samir; Francis, Wagdy; Girgis, Fouad Y.; Safwat, Mohamed; Lee, Young J.; Svennerholm, Ann-Mari; Clemens, John D.; Savarino, Stephen J.

CORPORATE SOURCE: U.S. Naval Medical Research Unit No. Three, Cairo, Egypt

SOURCE: Infection and Immunity (2001), 69(5), 2853-2857
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We assessed serol. responses to an oral, killed whole-cell **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B**-subunit (**ETEC**-rCTB) vaccine in 73 Egyptian adults, 105 school children, and 93 preschool children. Each subject received two doses of vaccine or placebo 2 wk apart, giving blood before immunization and 7 days after each dose. Plasma antibodies to rCTB and four vaccine-shared colonization factors (CFs) were measured by ELISA. IgA antibodies to rCTB and **CFA/I** were measured in all subjects, and those against **CS1**, **CS2**, and **CS4** were measured in all children plus a subset of 33 adults. IgG antibodies to these five antigens were measured in a subset of 30 to 33 subjects in each cohort. Seroconversion was defined as a > 2-fold increase in titer after vaccination. IgA and IgG seroconversion to rCTB was observed in 94 to 95% of adult vaccinees, with titer increases as robust as those previously reported for these two pediatric cohorts. The proportion showing IgA seroconversion to each CF antigen among vaccinated children (range, 70 to 96%) and adults (31 to 69%), as well as IgG seroconversion in children (44 to 75%) and adults (25 to 81%), was significantly higher than the corresponding proportion in placebo recipients, except for IgA responses to CS2 in adults. IgA anti-CF titers peaked after one dose in children, whereas in all age groups IgG antibodies rose incrementally after each dose. Independently, both preimmunization IgA titer and age were inversely related to the magnitude of IgA responses. In conclusion, serol. responses to the ETEC-rCTB vaccine may serve as practical immune outcome measures in future pediatric trials in areas where ETEC is endemic.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 04 Apr 2001
ACCESSION NUMBER: 2001:236341 HCAPLUS
DOCUMENT NUMBER: 135:342888
TITLE: Dose-dependent circulating immunoglobulin A antibody-secreting cell and serum antibody responses in Swedish volunteers to an oral inactivated **enterotoxigenic** Escherichia **coli** vaccine
AUTHOR(S): Jertborn, Marianne; Ahren, Christina; Svennerholm, Ann-Mari
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, Goteborg University, Goteborg, 413

46, Swed.
SOURCE: Clinical and Diagnostic Laboratory Immunology (2001), 8(2), 424-428
CODEN: CDIMEN; ISSN: 1071-412X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The immunogenicity of different prepns. of an oral inactivated **enterotoxigenic** Escherichia **coli** (**ETEC**) vaccine was evaluated in Swedish volunteers previously unexposed to **ETEC** infection. The vaccine prepns. consisted of recombinant **cholera** toxin **B** subunit (**CTB**) and various amts. of formalin-killed whole bacteria expressing the most prevalent colonization factor antigens (CFAs). Significant IgA antibody-secreting cell (ASC) responses against **CTB** and the various CFA components were seen in a majority of volunteers after two doses of ETEC vaccine independent of the vaccine lot given. The IgA ASC responses against **CTB** were significantly higher after the second than after the first immunization, whereas the CFA-specific IgA ASC responses were almost comparable after the first and second doses of ETEC vaccine. Two immunizations with one-third of a full dose of CFA-ETEC bacteria induced lower frequencies of IgA ASC responses against all the different CFAs than two full vaccine doses, i.e., 63 vs. 80% for **CFA/I**, 56 vs. 70% for **CS1**, 31 vs. 65% for **CS2**, and 56 vs. 75% for **CS4**. The proportion of vaccines responding with rises in the titer of serum IgA antibody against the various CFA antigens was also lower after immunization with the reduced dose of CFA-ETEC bacteria. These findings suggest that measurements of circulating IgA ASCs can be used not only for qual. but also for quant. assessments of the immunogenicity of individual fimbrial antigens in various prepns. of ETEC vaccine.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 22 Mar 2001
ACCESSION NUMBER: 2001:197353 HCAPLUS
TITLE: The Use of Attenuated Shigella Vaccine Strains to Deliver Heterologous Antigens and DNA Vaccines
AUTHOR(S): Barry, Eileen M.; Altboum, Zeev; Anderson, Richard; Pasetti, Marcela; Levine, Myron M.
CORPORATE SOURCE: Center for Vaccine Development, University of Maryland, Baltimore, MD, 21201, USA
SOURCE: Abstracts of Papers - American Chemical Society (2001), 221st, BIOT-046
CODEN: ACSRAL; ISSN: 0065-7727
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English

AB Attenuated strains of Shigella have been developed as live oral vaccines against shigellosis. With further genetic manipulation these strains have been used to express heterologous antigens from other pathogens and deliver these antigens to the host immune

system. Attenuated S. flexneri strain CVD 1204 has been used to create a multivalent hybrid Shigella/**enterotoxigenic** E. **coli** (**ETEC**) vaccine. Expression plasmids have been constructed to allow the stable expression of four different ETEC fimbrial antigens including **CFA/I**, **CS2**, **CS3**, and **CS4** as well as detoxified **heat labile** toxin individually in CVD 1204. Addnl. constructions have been designed encoding multiple operons to direct expression of two antigens in a single Shigella strain. In a mucosal immunization model in guinea pigs, serum IgG and mucosal IgA responses were elicited against each ETEC antigen and the Shigella vector strain itself and immunized guinea pigs were protected against challenge with wild type Shigella. In addition, these strains have been investigated as an alternative method for the delivery of DNA vaccine plasmids to the host. In a model system, fragment C of tetanus toxin encoded on a eukaryotic expression plasmid was delivered by attenuated Shigella strain CVD 1204 to guinea pigs by mucosal immunization. The Shigella-delivered DNA vaccine was able to elicit anti-fragment C antibody titers comparable to those elicited by CVD 1204 expressing fragment C by a prokaryotic expression system as well as engendering protection against wild type Shigella challenge.

L16 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 01 Aug 2000
ACCESSION NUMBER: 2000:519976 HCAPLUS
DOCUMENT NUMBER: 133:227633
TITLE: Safety and immunogenicity of two different lots of the oral, killed **enterotoxigenic** Escherichia **coli-cholera** toxin **B** subunit vaccine in Israeli young adults
AUTHOR(S): Cohen, Dani; Orr, Nadav; Haim, Moti; Ashkenazi, Shai; Robin, Guy; Green, Manfred S.; Ephros, Moshe; Sela, Tamar; Slepon, Raphael; Ashkenazi, Isaac; Taylor, David N.; Svennerholm, Ann-Mari; Eldad, Arieh; Shemer, Joshua
CORPORATE SOURCE: Army Health Branch Research Unit, Medical Corps, Israel Defence Force, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv-Jaffa, Israel
SOURCE: Infection and Immunity (2000), 68(8), 4492-4497
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Enterotoxigenic** Escherichia **coli** (**ETEC**) is one of the leading causes of diarrhea among Israeli soldiers serving in field units. Two double-blind placebo-controlled, randomized trials were performed among 155 healthy volunteers to evaluate the safety and immunogenicity of different lots of the oral, killed ETEC vaccine consisting of two doses of whole cells plus recombinantly produced **cholera** toxin **B** subunit (rCTB). The two doses of vaccine lot E005 and the first dose of vaccine lot E003 were well tolerated by the volunteers. However, 5 (17%) vaccinees reported an episode of vomiting a few

hours after the second dose of lot E003; none of the placebo recipients reported similar symptoms. Both lots of vaccine stimulated a rate of significant antibody-secreting cell (ASC) response to **CTB** and to colonization factor antigen I (CFA/I) after one or two doses, ranging from 85 to 100% and from 81 to 100%, resp. The rate of ASC response to **CS2**, **CS4**, and **CS5** was slightly lower than the rate of ASC response induced to **CTB**, **CFA/I**, and **CS1**. The second vaccine dose enhanced the response to **CTB** but did not increase the frequencies or magnitude of ASC responses to the other antigens. The two lots of the ETEC vaccine induced similar rates of serum antibody responses to **CTB** and CFA/I which were less frequent than the ASC responses to the same antigens. Based on these safety and immunogenicity data, an efficacy study of the ETEC vaccine is under way in the Israel Defense Force.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 30 Jun 2000
ACCESSION NUMBER: 2000:441654 HCAPLUS
DOCUMENT NUMBER: 133:64009
TITLE: Oral vaccine against diarrhea
INVENTOR(S): Carlin, Nils; Askelof, Per; Bjare, Ulf
PATENT ASSIGNEE(S): SBL Vaccin AB, Swed.
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037106	A1	20000629	WO 1999-SE2306	19991209
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
SE 9804415	A	20000619	SE 1998-4415	19981218
SE 515285	C2	20010709		
BR 9916278	A	20010904	BR 1999-16278	19991209
EP 1140159	A1	20011010	EP 1999-964847	19991209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EE 200100309	A	20020815	EE 2001-309	19991209
JP 2002532562	T2	20021002	JP 2000-589216	19991209
ZA 2001004362	A	20020114	ZA 2001-4362	20010528
HR 2001000433	A1	20020630	HR 2001-433	20010608

NO 2001002889 A 20010612 NO 2001-2889 20010612
PRIORITY APPLN. INFO.: SE 1998-4415 A 19981218
WO 1999-SE2306 W 19991209

AB An oral vaccine composition against **enterotoxigenic** E. **coli** caused diarrhea in humans is disclosed. It comprises a defined amount of at least three different types of colonization factor antigens (CFAs), e.g. 100 to 300 μg of each type, selected from the group consisting of **CFA I, CFA II** (**CS1, CS2** and **CS3**) and **CFA IV** (**CS4, CS5** and **CS6**), on killed E. coli bacteria lacking the gene encoding the **heat labile enterotoxin** (**LT**-), together with a defined amount of the **B**-subunit of **cholera toxin** (**CTB**), e.g. 0.5-2.0 mg, and a vehicle, such as PBS, which vaccine composition is purified from possible **heat stable enterotoxin** (**ST**).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 31 Jan 2000
ACCESSION NUMBER: 2000:74547 HCAPLUS
DOCUMENT NUMBER: 132:248318
TITLE: Prevalence of toxin types and colonization factors in **enterotoxigenic** Escherichia **coli** isolated during a 2-year period from diarrheal patients in Bangladesh
AUTHOR(S): Qadri, Firdausi; Das, Swadesh Kumar; Faruque, A. S. G.; Fuchs, George J.; Albert, M. John; Sack, R. Bradley; Svennerholm, Ann-Mari
CORPORATE SOURCE: Laboratory Sciences Division, ICDDR, Dhaka, 1000, Bangladesh
SOURCE: Journal of Clinical Microbiology (2000), 38(1), 27-31
CODEN: JCMIDW; ISSN: 0095-1137
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The prevalence of toxin types and colonization factors (CFs) of **enterotoxigenic** Escherichia **coli** (**ETEC**) was prospectively studied with fresh samples (n = 4,662) obtained from a 2% routine surveillance of diarrheal stool samples over 2 yr, from Sept. 1996 to August 1998. Stool samples were tested by enzyme-linked immunoassay techniques and with specific monoclonal antibodies for the toxins and CFs. The prevalence of ETEC was 14% (n = 662), with over 70% of the strains isolated from children 0 to 5 yr of age, of whom 93% were in the 0- to 3-yr-old age range. Of the total ETEC isolates, 49.4% were pos. for the **heat-stable toxin** (**ST**), 25.4% were pos. for the **heat-labile toxin** (**LT**) only, and 25.2% were pos. for both **LT** and **ST**. The rate of ETEC isolation peaked in the hot summer months of May to Sept. and decreased in winter. About 56% of the samples were pos. for 1 or more of the 12 CFs that were screened for. The coli

surface antigens **CS4**, **CS5**, and/or **CS6** of the **colonization factor antigen** (**CFA**)/**IV** complex were most prevalent (incidence, 31%), followed by **CFA/I** (23.5%) and coli surface antigens **CS1**, **CS2**, and **CS3** of **CFA/II** (21%). In addition, other CFs detected in decreasing order were CS7 (8%), CS14 (PCFO166) (7%), CS12 (PCFO159) (4%), CS17 (3%), and CS8 (CFA/III) (2.7%). The ST- or LT- and ST-pos. ETEC isolates expressed the CFs known to be the most prevalent (i.e., CFA/I, CFA/II, and CFA/IV), while the strains pos. for LT only did not. Among children who were infected with ETEC as the single pathogen, a trend of relatively more severe disease in children infected with ST-pos. ($P < 0.001$) or LT- and ST-pos. ($P < 0.001$) ETEC isolates compared to the severity of the disease in children infected with LT only-pos. ETEC isolates was seen. This study supports the fact that ETEC is still a major cause of childhood diarrhea in Bangladesh, especially in children up to 3 yr of age, and that measures to prevent such infections are needed in developing countries.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 30 Sep 1998
ACCESSION NUMBER: 1998:615639 HCAPLUS
DOCUMENT NUMBER: 130:22754
TITLE: Epidemiology and properties of **heat-stable enterotoxin**-producing Escherichia **coli** serotype O169:H41
AUTHOR(S): Nishikawa, Y.; Helander, A.; Ogasawara, J.; Moyer, N. P.; Hanaoka, M.; Hase, A.; Yasukawa, A.
CORPORATE SOURCE: Department of Epidemiology, Osaka City Institute of Public Health and Environmental Sciences, Osaka, 543-0026, Japan
SOURCE: Epidemiology and Infection (1998), 121(1), 31-42
CODEN: EPINEU; ISSN: 0950-2688
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Enterotoxigenic** Escherichia **coli** (**ETEC**) serotype O169:H41 organisms have become the most prevalent **ETEC** in Japan since the first outbreak in 1991. It was assumed that the outbreaks were due to clonal spread of this new ETEC serotype. The relationship of 32 strains isolated from 6 outbreaks were examined for biotype, antibiotic susceptibility, enterotoxigenicity, protein banding pattern, lipopolysaccharide banding pattern, plasmid anal., and ribotyping. Further, the strains were examined by hemagglutination, surface hydrophobicity, and the ability to adhere to HEp-2 cells. The present study suggests that the outbreaks were caused by multiple clones of STp-producing O169:H41 since they showed differences in ribotype and outer membrane protein banding patterns. The strains did not agglutinate human or bovine red blood cells in a mannose-resistant manner. They adhered to HEp-2 cells in a manner resembling enteroaggregative E.

coli. Five strains were examined by dot-blot tests for the **colonization factor antigens CFA /I, CS1, CS2, CS3, CS4, CS5, CS6,** CS7, PCFO159, PCFO166 and CFA/III. Although four strains expressed CS6, no structure for CS6 was identified. A strain that the anti-CS6 MAbs did not react with could adhere to HEp-2 cells in a mannose resistant manner; thus, it is unlikely that CS6 play an important role in the adhesion to the cells. Electron microscopy studies of the 0169:H41 strains suggested that curly fimbriae, a possible new colonization factor, may play an important role in the adhesion of the bacteria to HEp-2 cells. In conclusion, outbreaks due to ETEC 0169:H41 were caused by multiple clones, and the strains should be examined in detail for a possible new colonization factor.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 29 Jan 1998
ACCESSION NUMBER: 1998:50413 HCAPLUS
DOCUMENT NUMBER: 128:113817
TITLE: Safety and immunogenicity of an oral inactivated **enterotoxigenic** Escherichia **coli** vaccine
AUTHOR(S): Jertborn, Marianne; Ahren, Christina; Holmgren, Jan; Svennerholm, Ann-Mari
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, Goteborg University, Goteborg, S-413 46, Swed.
SOURCE: Vaccine (1998), 16(2/3), 255-260
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The safety and immunogenicity of two different lots, 001 and 003, of an oral inactivated **enterotoxigenic** Escherichia **coli** (**ETEC**) vaccine consisting of a mixture of formalin-killed whole bacteria expressing the most prevalent colonization factor antigens, i.e. CFA/I, CFA/II and CFA/IV and recombinantly produced **cholera B** subunit (rCTB) have been evaluated in Swedish volunteers. Neither of the two vaccine prepns., containing different CFA/II-expressing strains but otherwise identical, gave rise to any significant side-effects. Mucosal immune responses, as reflected in antibody-secreting cell (ASC) responses in peripheral blood, were studied after two doses of vaccine and did not differ significantly for the two vaccine lots. Vaccination induced high levels of **CTB**-specific IgA ASCs in 100% of the volunteers, and significant IgA ASC responses (9- to 36-fold) were noted in 84% of them against **CFA/I**, in 87% against **CFA/II** subcomponents **CS1-CS3** and in 91% against **CFA/IV** subfactors **CS4** and/or **CS5**. The frequencies and magnitudes of CFA IgA ASC responses were similar when giving the vaccine with a 1 or 2 wk interval. Results from serol. analyses showed that the local IgA responses against CFAs are

only infrequently associated with serum antibody titer rises.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 03 Apr 1996
ACCESSION NUMBER: 1996:190721 HCAPLUS
DOCUMENT NUMBER: 124:252012
TITLE: Detection of the enteroaggregative Escherichia **coli heat-stable enterotoxin** 1 gene sequences in **enterotoxigenic** E. **coli** strains pathogenic for humans
AUTHOR(S): Yamamoto, Tatsuo; Echeverria, Peter
CORPORATE SOURCE: Research Institute, International Medical Center of Japan, Tokyo, Japan
SOURCE: Infection and Immunity (1996), 64(4), 1441-5
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The sequence of the enteroaggregative Escherichia **coli enterotoxin** 1 (EAST1) gene was present in most (or all) strains of human-colonizing **enterotoxigenic** E. **coli** (**ETEC**) with **colonization factor antigen II** (**CFA/II**) or **CFA/IV** (**CS6**). The EAST1 gene was also strongly associated with PCFO9+ ETEC or CFA/I+ ETEC elaborating **heat-labile** enterotoxin (and **heat-stable** enterotoxin I). In contrast, CFA/I+ ETEC elaborating **heat-stable** enterotoxin I, CFA/III+ ETEC, or CS17+ ETEC exhibited very weak or no association E. coli from healthy volunteers had no EAST1 gene sequence. A CFA/I+ ETEC strain (H10407) possessed multiple copies of the EAST1 gene on the CFA/I-encoding plasmid and chromosome. In one CFA/II+ ETEC strain, the EAST1 gene was present on the CFA/II-encoding plasmid. The EAST1 gene sequences of the CFA/I+ and CFA/II+ **ETEC** strains were identical to each other and 99.1% homologous to the reported gene sequence of enteroaggregative E. **coli**. The data indicate that the EAST1 gene is distributed among ETEC strains with a case of the presence of multiple copies in a single cell and that this distribution is associated with the adherence factor type.

L16 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 26 Nov 1994
ACCESSION NUMBER: 1994:650836 HCAPLUS
DOCUMENT NUMBER: 121:250836
TITLE: Prevalence of colonization factor antigens (CFAs) and adherence to HeLa cells in **enterotoxigenic** Escherichia **coli** isolated from feces of children in Sao Paulo
AUTHOR(S): Guth, Beatriz Ernestina Cabilio; Aguiar, Eliana Goncalves; Griffin, Patricia Marie; Ramos, Sonia Regina Testa da Silva; Gomes, Tania Aparecida Tardelli

CORPORATE SOURCE: Dep. Microbiol., Immunol. Parasitology, Escola Paulista de Med., Sao Paulo, 04023-062, Brazil
SOURCE: Microbiology and Immunology (1994), 38(9), 695-701
CODEN: MIIMDV; ISSN: 0385-5600
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fifty-eight **enterotoxigenic** Escherichia **coli** (**ETEC**) strains, isolated from children with and without diarrhea in Sao Paulo, were examined for the presence of colonization factor antigens (CGAs) and their ability to adhere to HeLa cells. Antisera to **CFA/I**, the coli surface (CS) antigens CS1CS3, CS2CS3, **CS2** of **CFA/II**, CFA/III, and CS5CS6 and **CS6** of **CFA/IV** were used. CFAs were identified in 43% of the ETEC strains: 40% of the strains with **CFAs** harbored **CFA/I**, 24% carried **CFA/II** (CD1CS3), 24% carried **CFA/IV** (**CS6**), and 12% carried **CFA/IV** (CS5CS6). CFAs occurred mainly among ETEC strains producing only **heat-stable** (**ST**-I) **enterotoxin** and in strains also producing **heat-labile toxin** (**LT**-I). No ETEC strains tested expressed CFA/III. A marked change in serotypes of ST-I-producing strains was found in Sau Paulo between 1979 and 1990. Adherence to HeLa cells was detected in 14% of the ETEC strains. All of them had a diffuse adherence pattern and produced only ST-I, and 88% carried CD6 antigen.

L16 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 27 Dec 1991
ACCESSION NUMBER: 1991:675315 HCAPLUS
DOCUMENT NUMBER: 115:275315
TITLE: New adhesive factor (antigen 8786) on a human **enterotoxigenic** Escherichia **coli** O117:H4 strain isolated in Africa
AUTHOR(S): Aubel, Dominique; Darfeuille-Michaud, Arlette; Joly, Bernard
CORPORATE SOURCE: Serv. Bacteriol.-Virol., Fac. Pharm., Clermont-Ferrand, 63001, Fr.
SOURCE: Infection and Immunity (1991), 59(4), 1290-9
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Enterotoxigenic** E. **coli** 8786, of serotype O117:H4, produced only **heat-stable** enterotoxin and gave mannose-resistant hemagglutination with human and bovine erythrocytes. The strain adhered to the brush border of human enterocytes and to enterocytelike cell line Caco-2. Adhesion inhibition assays using Caco-2 cells with different adhesive factor exts. showed that the adhesive factor of E. coli 8786 is different from **colonization factor antigen I** (**CFA/I**), **CFA/II**, CFA/III of A. Darfeuille et al. (1983), **CS6**, and antigen 2230. A bacterial surface protein, designated antigen 8786, with a mol. mass of 16,000 Da was responsible for the adhesion to intestinal cells. It was immunol. different from previously

described adhesive factors as determined by immunoblotting. Antigen 8786 was detected on the bacterial cell surface and appeared to be nonfimbrial. NH2-terminal anal. of antigen 8786 showed no homol. with the previously described adhesive factors. Nevertheless, antigen 8786 is closely related to the NH2-terminal sequence of Salmonella enteritidis fimbrin. A hybridization experiment using a synthetic oligonucleotide probe based on the NH2-terminal amino acid sequence of antigen 8786 revealed that the coding region was located on a 70-MDa plasmid.

L16 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 14 Oct 1988
ACCESSION NUMBER: 1988:525664 HCAPLUS
DOCUMENT NUMBER: 109:125664
TITLE: Genetic control and properties of coli surface antigens of colonization factor antigen IV (PCF8775) of **enterotoxigenic** Escherichia **coli**
AUTHOR(S): McConnell, Moyra M.; Thomas, Linda V.; Willshaw, Geraldine A.; Smith, Henry R.; Rowe, Bernard
CORPORATE SOURCE: Div. Enteric Pathog., Cent. Public Health Lab., London, NW9 5HT, UK
SOURCE: Infection and Immunity (1988), 56(8), 1974-80
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Enterotoxigenic** E. **coli** producing **coli surface antigen 4** (**CS4**), **CS5**, and **CS6** of **colonization factor antigen IV** were examined This factor was originally called putative colonization factor 8775 (PCF8775). All of the coli surface antigens were plasmid-coded and were usually carried on the same plasmid as the genes coding for **heat-stable toxin** (**ST**) or **heat-labile toxin** (**LT**); thus, CS5-CS6-**ST**, CS6-**ST**, and CS6-**LT** plasmids were found. In strains of serotype O25:H42, the genes coding for CS4 and CS6 were on a plasmid sep. from that containing the genes coding for ST and LT. CS4 and CS5 were fimbrial antigens with a subunit mol. mass of about 17.0 and 21.0 kilodaltons (kDa), resp. CS6 was found as a single polypeptide with a mol. mass of about 14.5 kDa in strains of serotypes O25:H42, O27:H7, and O27:H20 when heated exts. were run on SDS-PAGE. CS6-pos. exts. of strains of serogroups O148, O159, and O167 showed 2 bands with mol. masses between 14.5 and 16.0 kDa.

L16 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 08 Feb 1986
ACCESSION NUMBER: 1986:32742 HCAPLUS
DOCUMENT NUMBER: 104:32742
TITLE: Enzyme-linked immunosorbent assays for the detection of adhesion factor antigens of **enterotoxigenic** Escherichia **coli**
AUTHOR(S): McConnell, M. M.; Thomas, L. V.; Day, N. P.; Rowe, B.
CORPORATE SOURCE: Div. Enteric Pathogens, Cent. Public Health

Lab., London, UK
SOURCE: Journal of Infectious Diseases (1985), 152(6), 1120-7
CODEN: JIDIAQ; ISSN: 0022-1899
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two hundred forty-four specimens of E. coli isolated in Bangladesh and Thailand and identified as enterotoxin producers were tested for the presence of adhesion antigens by mannose-resistant hemagglutination, immunodiffusion, and ELISA. Specific antisera to the **colonization factor antigen** (**CFA**)/**I**, **CFA/II** (consisting of E. coli surface antigens [**CS**] **1**, 2, and 3), and putative colonization factor antigen (PCF) 8775 (consisting of **CS4**, 5, and 6) were used in immunodiffusion tests and ELISAs. The antigens could be detected in more strains by ELISA than by immunodiffusion. Twenty-nine percent of specimens of E. coli from Thailand and 47% from Bangladesh carried an adhesion antigen. Many of the strains had lost the ability to produce enterotoxins. Forty percent of strains from Thailand and 64% from Bangladesh that were still enterotoxigenic carried adhesion factors. These antigens were found on strains with **heat-stable** and **heat-labile** enterotoxin but not on strains producing only **heat-labile** enterotoxin. PCF8775 antigens were associated mainly with strains from Bangladesh, where 10 strains that produced only CS6 were detected.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 11:32:08 ON 27 APR 2004)
L17 133 S L16
L18 39 DUP REM L17 (94 DUPLICATES REMOVED)

L18 ANSWER 1 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-301010 [29] WPIDS
CROSS REFERENCE: 2003-301009 [29]
DOC. NO. CPI: C2003-078603
TITLE: New Escherichia coli cell useful in manufacturing a medicament for vaccination against diarrhea, expresses **colonization factor antigen CFA/I**, **CS5** and/or **CS6** from a native plasmid, but does not express **heat stable** toxin.
DERWENT CLASS: B04 D16
INVENTOR(S): BEAVIS, J C; DARSLEY, M J; GREENWOOD, J; STEPHENS, J C; TURNER, A K
PATENT ASSIGNEE(S): (ACAM-N) ACAMBIS RES LTD
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003022307	A1	20030320	(200329)*	EN	51

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ
DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP
KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ
NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ
UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003022307	A1	WO 2002-GB4164	20020911

PRIORITY APPLN. INFO: GB 2001-21998 20010911
AN 2003-301010 [29] WPIDS
CR 2003-301009 [29]
AB WO2003022307 A UPAB: 20030505
NOVELTY - A bacterial cell which expresses **colonization factor antigen CFA/I,** **CS5** and/or **CS6** from a native plasmid, but does not express **heat stable toxin** (**ST**), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a native **enterotoxigenic** Escherichia **coli** plasmid in which the gene encoding **ST toxin** is deleted or inactivated and which encodes **colonization factor antigen CFA/I,** **CS5** and/or **CS6;**

(2) a vaccine against diarrhea, comprising the cell cited above and a carrier or diluent;

(3) vaccinating a mammal against diarrhea, comprising administering to the mammal the above cell or vaccine;

(4) a suicide vector which is less than 5 kb in size and comprises the sacB region which codes for a product that is toxic to bacteria when grown on sucrose, in which region the IS 1 insertion sequence is deleted or inactivated; and

(5) producing a bacterial cell in which a target gene is deleted, inactivated or replaced, comprising transferring the above vector into a bacterial cell containing the target gene and selecting for a cell in which the target gene has been deleted, inactivated or replaced.

ACTIVITY - Antibacterial; Antidiarrheal. No biological data is given.

MECHANISM OF ACTION - Vaccine.

USE - The cell is useful in manufacturing a medicament for vaccination against diarrhea (claimed).

Dwg.0/20

L18 ANSWER 2 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-301009 [29] WPIDS
CROSS REFERENCE: 2003-301010 [29]
DOC. NO. CPI: C2003-078602
TITLE: New bacterial cell expressing three or more coli surface antigens, useful for manufacturing a medicament, i.e. a vaccine, for vaccination against

diarrhea.

DERWENT CLASS: B04 D16
INVENTOR(S): BEAVIS, J C; DARSLEY, M J; GREENWOOD, J; STEPHENS, J C; TURNER, A K
PATENT ASSIGNEE(S): (ACAM-N) ACAMBIS RES LTD
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003022306	A2	20030320	(200329)*	EN	115

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003022306	A2	WO 2002-GB4123	20020911

PRIORITY APPLN. INFO: GB 2001-21998 20010911
AN 2003-301009 [29] WPIDS
CR 2003-301010 [29]
AB WO2003022306 A UPAB: 20030505
NOVELTY - A bacterial cell expressing three or more coli surface antigens, and deposited under accession number 02082969 at the ECACC, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a vaccine against diarrhea comprising:

(a) the bacterial cell cited above and a pharmaceutical carrier or diluent; or (b) bacterial cells which together express all of **colonization factor antigen** (**CFA**)/**I**, coli surface (**CS**)**1**, **CS2**, **CS3**, **CS4**, **CS5** and **CS6**, where the vaccine comprises fewer than five bacterial strains; and

(b) vaccinating a mammal against diarrhea comprising administering to the mammal the bacterial cell cited above or the vaccine of (1).

ACTIVITY - Antidiarrheic; Antibacterial. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The bacterial cell is useful for manufacturing a medicament, i.e. a vaccine, for vaccination against diarrhea (claimed). The vaccine is also useful for targeting bacterial infection.

Dwg.0/14

ANSWER 3 OF 39 MEDLINE on STN DUPLICATE 1
SION NUMBER: 2003225165 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12744870
TITLE: Safety and immunogenicity of an oral, inactivated **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B** subunit vaccine in Bangladeshi children 18-36 months of age.
AUTHOR: Qadri Firdausi; Ahmed Tanvir; Ahmed Firoz; Bradley Sack R; Sack David A; Svennerholm Ann Mari
CORPORATE SOURCE: Laboratory Sciences Division, International Centre for Diarrhoeal Disease Research, GPO Box 128, Dhaka 1000, Bangladesh.. fqadri@icddrb.org
SOURCE: Vaccine, (2003 Jun 2) 21 (19-20) 2394-403.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20030515
Last Updated on STN: 20040106
Entered Medline: 20040105

AB A phase II safety and immunogenicity study of an oral-formalin inactivated **enterotoxigenic** Escherichia **coli** (**ETEC**) vaccine containing six colonization factors (**CFA/I, CS1, CS2, CS3**, **CS4, CS5**) and 1mg of recombinant **cholera** toxin **B** subunit (the CF-BS-**ETEC** vaccine) was carried out in an urban slum of Dhaka city in Bangladesh. The study was carried out in a double blinded, placebo controlled design in 158 children, 18-36 months of age. Children were given two doses of the CF-BS-**ETEC** vaccine or the placebo which consisted of E. **coli** K12. The vaccine was well tolerated.The immune response was studied in 60 children (30 each in the placebo and vaccine group). Significant vaccine specific IgA antibody-secreting cell (ASC) responses were seen 7 days after ingestion of the first and second dose of the vaccine. The responses to **CFA/I** (P<or=0.001), **CS2** (P=0.021), **CS4** (P=0.009) and rCTB (P<or=0.001) were elevated in the vaccines in comparison to the pre-immune values and in comparison to those seen in the placebo recipients (P=0.018 to <0.001). Vaccines but not placebo recipients also showed significantly increased IgM ASC responses to all three CF antigens that were tested (P=0.012 to <0.001) and IgG-ASCs to rCTB (P<0.001). Peak ASC levels were reached after one dose of the vaccine with no further increase or decrease after the second dose.The vaccine recipients also responded with IgA plasma antibodies to **CFA/I, CS1, CS2, CS4** and rCTB after one or two doses of the vaccine (P=0.01 to <0.001). Subjects in the placebo group failed to mount responses to any of the antigens. The vaccine also induced responses in mucosal IgA antibodies in feces to **CFA/I, CS2** and rCTB (61, 88 and 69% responder frequency, respectively) and the magnitude of the response was elevated in comparison to the pre-immune levels (P=0.031 to <0.001) and to the levels of the control group (P=0.003 to <0.001).This study thus shows that the

CF-BS-ETEC vaccine is well tolerated in children, 18-36 months of age and gives rise to significant systemic and mucosal IgA antibody responses.

L18 ANSWER 4 OF 39 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003188859 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12706673
TITLE: Mucosal immunization of BALB/c mice using **enterotoxigenic** Escherichia **coli** colonization factors **CFA/I** and **CS6** administered with and without a mutant **heat-labile** enterotoxin.
AUTHOR: Byrd Wyatt; Cassels Frederick J
CORPORATE SOURCE: Department of Enteric Infections, Walter Reed Army Institute of Research, 503 Robert Grant Avenue, Silver Spring, MD 20910-7500, USA..
wyatt.byrd@na.amedd.army.mil
SOURCE: Vaccine, (2003 May 16) 21 (17-18) 1884-93.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20030423
Last Updated on STN: 20040122
Entered Medline: 20040121

AB Mice (BALB/c) were intranasally (IN) and intragastrically (IG) administered the ETEC colonization factors (CF), **CFA/I** and **CS6**, with and without the R192G mutant **heat-labile** enterotoxin (mLT), and immunogenicity and efficacy measured. The IN administration of CFA/I to mice induced strong serum and fecal IgG and IgA responses. The IG administration of CFA/I to mice induced serum IgG and fecal IgA responses, but only when mLT was co-administered with CFA/I were serum IgA titers detected. The IN administration of CS6 to mice induced serum IgG antibodies, and mLT, when co-administered with CS6, enhanced the serum IgG response. Only when the mLT was co-administered with CS6, were serum and fecal IgA responses detected. The IG administration of CS6 plus mLT induced serum IgG and fecal IgA responses. Partial protection against lethal challenge with ETEC strain H10407 was seen in the mice IN administered the CFA/I plus mLT ($P<0.01$), and H10407 was cleared from the lungs of CFA/I plus mLT-immunized mice at a significantly greater rate than from the control mice ($P<0.05$). **CFA/I** and **CS6** administered IN and IG induced mixed Th1/Th2 immune responses with the Th2 type being predominant as evidenced by IgG1>IgG2a. The administration of colonization factors to mice, particularly by the IN route, potentially serves as a useful way to measure the serum and mucosal immune responses to these antigens prior to their use in volunteers.

L18 ANSWER 5 OF 39 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2003025547 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12531629
TITLE: Immune responses elicited against multiple

enterotoxigenic Escherichia **coli** fimbriae and mutant LT expressed in attenuated Shigella vaccine strains.

AUTHOR: Barry Eileen M; Altboum Zeev; Losonsky Genevieve; Levine Myron M

CORPORATE SOURCE: Center for Vaccine Development, University of Maryland, 685 West Baltimore Street, Baltimore, MD 21201, USA.. ebarry@umaryland.edu

CONTRACT NUMBER: R01-AI29471 (NIAID)

SOURCE: Vaccine, (2003 Jan 17) 21 (5-6) 333-40.
Journal code: 8406899. ISSN: 0264-410X.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200309

ENTRY DATE: Entered STN: 20030118
Last Updated on STN: 20030903
Entered Medline: 20030902

AB Shigella and **enterotoxigenic** Escherichia **coli** (**ETEC**) continue to be important causes of diarrheal disease in infants and young children in developing countries and are major etiologic agents of traveler's diarrhea. Since attenuated strains of Shigella have been developed as live oral vaccines against shigellosis, we have adapted these attenuated Shigella strains to serve as carriers of ETEC antigens, thereby constituting a hybrid vaccine. Since protective immunity against ETEC is largely directed against fimbrial antigens (of which there are multiple antigenic types), we have individually expressed four different ETEC fimbriae, including **CFA/I**, **CS2**, **CS3**, and **CS4**, using deltaguaBA attenuated Shigella vaccine strain CVD 1204 as a prototype live vector. Following mucosal (intranasal) immunization of guinea pigs, serum IgG and mucosal IgA responses were elicited against each fimbrial type. An additional strain was constructed expressing a detoxified version of the human ETEC variant of **heat labile** toxin (LThK63). Following mucosal immunization of guinea pigs with a mixed inoculum containing five Shigella strains each expressing a different ETEC antigen, immune responses were observed against each ETEC antigen plus the Shigella vector.

L18 ANSWER 6 OF 39 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2003102543 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12614980

TITLE: Development and evaluation of genotypic assays for the detection and characterization of **enterotoxigenic** Escherichia **coli**.

AUTHOR: Steinsland Hans; Valentiner-Branth Palle; Grewal Harleen M S; Gaastra Wim; Molbak K Kare; Sommerfelt Halvor

CORPORATE SOURCE: Centre for International Health, University of Bergen, Norway.. hans.steinsland@bio.uib.no

SOURCE: Diagnostic microbiology and infectious disease, (2003 Feb) 45 (2) 97-105.
Journal code: 8305899. ISSN: 0732-8893.

PUB. COUNTRY: United States

DOCUMENT TYPE: (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20030305
Last Updated on STN: 20030429
Entered Medline: 20030428

AB We developed and evaluated a method to genotypically identify **enterotoxigenic** Escherichia **coli** (**ETEC**) and to characterize these organisms with respect to 18 of 21 known colonization factors (CFs). The method, which is based on polynucleotide DNA-DNA colony hybridization, includes a pooled **toxin** probe assay to identify ETEC, and individual probe assays to detect the **enterotoxins** STp, STh, and **LT**, and the CFs **CFA/I**, **CS1**-CS8, CS12-CS15, CS17-CS19, CS21, and CS22. We evaluated the pooled toxin probe assay during a cohort study of childhood diarrhea, and the individual probe assays against 33 reference strains and 92 clinical ETEC isolates. There was close to a complete agreement between the pooled toxin probe assay and the individual toxin probe assays, and between the individual CF probe assays and the corresponding phenotypic assays.

L18 ANSWER 7 OF 39 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2002733726 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12496144
TITLE: Pathogenicity and immune response measured in mice following intranasal challenge with **enterotoxigenic** Escherichia **coli** strains H10407 and B7A.
AUTHOR: Byrd Wyatt; Mog Steven R; Cassels Frederick J
CORPORATE SOURCE: Department of Enteric Infections, Walter Reed Army Institute of Research, Silver Spring, Maryland 20910-7500, USA.. wyatt.byrd@na.amedd.army.mil
SOURCE: Infection and immunity, (2003 Jan) 71 (1) 13-21. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20021227
Last Updated on STN: 20030211
Entered Medline: 20030210

AB The pathogenicity and immunogenicity induced in BALB/c mice by intranasal (i.n.) inoculation of **enterotoxigenic** Escherichia **coli** (**ETEC**) strains H10407 (O78:H11:**CFA/I**:LT(+):ST(+)) and B7A (O148:H28:**CS6**:LT(+):ST(+)) (two **ETEC** strains previously used in human challenge trials) were studied. The i.n. inoculation of BALB/c mice with large doses of ETEC strains H10407 and B7A caused illness and death. The H10407 strain was found to be consistently more virulent than the B7A strain. Following i.n. challenge with nonlethal doses of H10407 and B7A, the bacteria were cleared from the lungs of the mice at a steady rate over a 2-week period. Macrophages and

neutrophils were observed in the alveoli and bronchioles, and lymphocytes were observed in the septa, around vessels, and in the pleura of the lungs in mice challenged with H10407 and B7A. In mice i.n. challenged with H10407, serum immunoglobulin G (IgG) and IgM antibodies were measured at high titers to the CFA/I and O78 lipopolysaccharide (LPS) antigens. In mice i.n. challenged with B7A, low serum IgG antibody titers were detected against CS6, and low serum IgG and IgM antibody titers were detected against O148 LPS. The serum IgG and IgM antibody titers against the **heat -labile** enterotoxin were equivalent in the H10407- and B7A-challenged mice. The CFA/I and O78 LPS antigens gave mixed T-helper cell 1-T-helper cell 2 (Th1-Th2) responses in which the Th2 response was greater than the Th1 response (i.e., stimulated primarily an antibody response). These studies indicate that the i.n. challenge of BALB/c mice with ETEC strains may provide a useful animal model to better understand the immunogenicity and pathogenicity of ETEC and its virulence determinants. This model may also be useful in providing selection criteria for vaccine candidates for use in primate and human trials.

L18 ANSWER 8 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2003:509786 BIOSIS
DOCUMENT NUMBER: PREV200300509069
TITLE: Detection of **enterotoxigenic** Escherichia **coli**-specific secretory IgA in breast milk of mothers from Abu Homos Egypt.
AUTHOR(S): El-Mohamady, H. [Reprint Author]; Francis, W. M. [Reprint Author]; Rockabrand, D. M. [Reprint Author]; Rozmajzl, P. J. [Reprint Author]; Wierzba, T. F. [Reprint Author]; Savarino, S. J.; Clemens, J. D.; Svennerholm, A. M.; Frenck, R. W. [Reprint Author]
CORPORATE SOURCE: Naval Medical Research Unit No. 3, Cairo, Egypt
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. C-395. http://www.asmusa.org/mtgsrc/generalmeeting.htm. cd-rom.
Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology. ISSN: 1060-2011 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Oct 2003
Last Updated on STN: 29 Oct 2003

AB Background: Breast milk provides an ideal nutrient composition for the newborn and contains a variety of substances that may actively influence neonatal protection against gastrointestinal diseases. Studies of the epidemiology of diarrhea and breast-feeding have shown that infants who are breast-fed have a lower incidence of diarrhea than those who are fed formula. This study aimed at testing human breast milk for the presence of secretory IgA (sIgA) specific for **enterotoxigenic** Escherichia **coli** (**ETEC**) **heat labile-toxin** (**LT**) and **colonization factor**

antigens CFA/I and **CS6**.
Methods: Breast milk samples were collected from mothers who were participating in a birth cohort study for diarrheal disease surveillance in Lower Egypt. Samples were assayed by ELISA for sIgA antibodies against **CS6** (n=193), LT (n=471) and **CFA /I** (n=164). Samples were considered positive that demonstrated a >3-fold rise in titer compared to those that were ELISA negative at dilutions of 1:2. Results: More than fifty percent of samples (n=83) had anti-CFA/I antibody titers of >5 (a range of 5-568). Antibodies specific for CS6 and LT were detected in 73% and 56.5% of the breast milk samples, respectively. The ELISA results were confirmed by Western blotting and immuno-dotblot experiments using the respective antigenic preparations and whole bacteria isolates, respectively. Conclusion: The results indicate the potential role of passively transferred ETEC-specific sIgA antibodies through breast feeding to either engender immunity to ETEC infection in infants or reduce the severity of infectious diarrhea. Future studies, including dose response inhibition of in vitro bacterial adhesion to Caco-2 cell line by preincubation of bacteria with breast milk, are planned to demonstrate the protective role, if any, of these antibodies.

L18 ANSWER 9 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2003:519158 BIOSIS
DOCUMENT NUMBER: PREV200300520627
TITLE: Development of non-human primate animal models for **enterotoxigenic** Escherichia **coli** (**ETEC**) diarrhea and vaccine testing.
AUTHOR(S): Hall, E. R. [Reprint Author]; Cassels, F.; Jones, F.; Diaz-Mayoral, N. [Reprint Author]; Caoili, G. [Reprint Author]; Wolf, M.; Scott, D. [Reprint Author]; Savarino, S. [Reprint Author]
CORPORATE SOURCE: Naval Medical Research Center, Silver Spring, MD, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. D-173. http://www.asmusa.org/mtgsrc/generalmeeting.htm. cd-rom.
Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology. ISSN: 1060-2011 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Nov 2003
Last Updated on STN: 5 Nov 2003

AB Studies were conducted to evaluate Macaca mulatta (rhesus) monkeys as a possible animal model for studying ETEC diarrhea. Four groups of adult rhesus monkeys (n=5 monkeys/dose group) were challenged intragastrically with 5X1010 and 5X1012 colony forming units (cfu) of ETEC strain B7A (LT/ST+, **CS6**+) or H10407 (LT/ST+, **CFA/I**+) after peroral administration CeraVacx buffer and a histamine-2 (H2)-receptor antagonist to neutralize stomach acidity. Fecal excretion of E. coli was monitored daily after challenge by stool culture on MacConkey agar. The identity of

presumptive ETEC was confirmed by colony immunoblots. Monkeys were examined twice daily for a period 10 days for evidence of diarrhea. Blood samples were collected before and 7, 14 and 21 after challenge. ETEC-specific mucosal and systemic immune responses were assessed by measurement of anti-colonization factor antigen (CFA) and **heat-labile toxin** (**LT**)
antibody secreting cells (ASC) in peripheral blood, as well as plasma antibody levels. Two of 5 (40%) and 3 of 5 (60%) monkeys developed diarrhea after challenge with 5X1012 colony forming units (cfu) of ETEC strains B7A and H10407, respectively. No diarrhea was observed in monkeys receiving a lower dose (5X1010 cfu) of either challenge strain. All monkeys excreted the ETEC challenge strain in their stool for at least 48 hrs, with 60% or greater shedding past 3 days. Immune responses to ETEC antigens were detected in the majority of B7A (80%) and H10407 (100%) 5X1012 cfu challenged monkeys, indicating a promising model for preclinical immunogenicity testing of ETEC vaccine candidates. For comparison, we have begun ETEC challenge experiments in owl monkeys (Aotus nancymae). These animals have a diarrhea attack rate of 60% following oral challenge with 5X1010 ETEC H10407 and the level of colonization correlates well with diarrhea episodes. Combined, our preliminary data indicate that less bacteria are required to cause an attack rate of 60% in Aotus than Rhesus monkeys. Further studies are planned to determine if 5X1011 ETEC will result in the target attack rate of 80% in Aotus monkeys, an important endpoint for future vaccine efficacy trials.

L18 ANSWER 10 OF 39 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 2002371116 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12089285
TITLE: Prevalence of **enterotoxigenic** Escherichia **coli** strains harboring the longus pilus gene in Brazil.
AUTHOR: Nishimura Lucilia S; Giron Jorge A; Nunes Solange L; Guth Beatriz E C
CORPORATE SOURCE: Departamento de Microbiologia, Imunologia e Parasitologia, Universidade Federal de Sao Paulo Escola Paulista de Medicina, UNIFESP, Sao Paulo, Brazil.
SOURCE: Journal of clinical microbiology, (2002 Jul) 40 (7) 2606-8.
Journal code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020716
Last Updated on STN: 20020827
Entered Medline: 20020826

AB The longus type IV pilus gene (lngA) was highly prevalent (32.8%) among Brazilian **enterotoxigenic** Escherichia **coli** strains producing both **heat-labile** and **heat-stable** enterotoxins and bearing the **CFA/I**, CS1CS3, or **CS6** antigen.
Furthermore, lngA was more often found in strains isolated from

children with diarrhea than in strains isolated from children without diarrhea.

L18 ANSWER 11 OF 39 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2002246664 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11985274
TITLE: Simultaneous expression of CS3 colonization factor antigen and **LT**-B/**ST** fusion **enterotoxin** antigen of **enterotoxigenic** Escherichia **coli** by attenuated Salmonella typhimurium.
AUTHOR: Xu Bing; Zhang Zhao-Shan; Li Shu-Qin; Shu Dong; Huang Cui-Fen
CORPORATE SOURCE: Beijing Institute of Biotechnology, 20 Dong Dajie Street, Fengtai District, Beijing 100071, China.. bingxx@hotmail.com
SOURCE: Yi chuan xue bao = Acta genetica Sinica, (2002 Apr) 29 (4) 370-6.
Journal code: 7900784. ISSN: 0379-4172.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020503
Last Updated on STN: 20020517
Entered Medline: 20020516

AB **LT** and **ST** are the main **enterotoxins** of **enterotoxigenic** Escherichia **coli** (**ETEC**) found in clinical isolates, and **CS3** (the common antigen in the **CFA/II** family of fimbrial antigens) is one of the most prevalent antigens of colonization factors. The genetic determinants encoding CS3 and **LT**-B/**ST** fusion **toxin** were manipulated so that these important antigens are expressed simultaneously in attenuated Salmonella typhimurium oral vaccine strain X4072. These antigens produced by X4072 (pXZL88) could be recognized with monospecific CS3, LT or ST antibodies respectively. The specific antibodies against CS3, LT and ST could be detected. In the sera of immunized mice via oral route with the live bacteria. Significantly, the antibody to ST was able to neutralize the biological activity of native ST. This prototype construct may be proved to be useful in investigating the live vector approach to immunoprophylaxis of ETEC diarrhea disease.

L18 ANSWER 12 OF 39 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2002332604 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12075764
TITLE: Introductory evaluation of an oral, killed whole cell **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B** subunit vaccine in Egyptian infants.
AUTHOR: Savarino Stephen J; Hall Eric R; Bassily Samir; Wierzba Thomas F; Youssef Fouad G; Peruski Leonard F Jr; Abu-Elyazeed Remon; Rao Malla; Francis Wagdy M; El Mohamady Hanan; Safwat Mohammed; Naficy Abdollah B; Svennerholm Ann-Mari; Jertborn Marianne; Lee Young

J; Clemens John D
CORPORATE SOURCE: US Naval Medical Research Unit Number 3, Cairo, Egypt. (Pride Study Group). savarinos@nmrc.navy.mil
CONTRACT NUMBER: Y1-HD-0026-01 (NICHD)
SOURCE: Pediatric infectious disease journal, (2002 Apr) 21 (4) 322-30.
Journal code: 8701858. ISSN: 0891-3668.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020623
Last Updated on STN: 20030403
Entered Medline: 20021016

AB BACKGROUND: We conducted the first trial to assess the safety and immunogenicity of an oral, killed **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B** -subunit vaccine in children <2 years old. METHODS: Three doses of vaccine or killed E. coli K-12 control were given at 2-week intervals to 64 Egyptian infants, 6 to 18 months old, in a randomized, double blind manner. Adverse events were monitored for 3 days after each dose. Blood was collected before immunization and 7 to 10 days after each dose to assess vaccine-specific serologic responses. RESULTS: There was no statistically significant intergroup difference in the percentage of subjects reporting the primary safety endpoint (diarrhea or vomiting) after the first (31%, vaccine; 30%, control) or third (14%, vaccine; 18%, control) dose, whereas there was a trend toward greater reporting in the vaccine group after Dose 2 (36%, vaccine; 18%, control; P = 0.052). The percentage of children showing IgA seroconversion after any dose was higher in the vaccine than the control group for recombinant **cholera** toxin **B**-subunit (97% vs. 46%), **colonization factor antigen I** (61% vs. 18%) and coli **surface antigen 4** (39% vs. 4%) (P < 0.001 for each comparison). IgG seroconversion rates in the vaccine and control groups were 97 and 21% to recombinant **cholera** toxin **B**-subunit (P < 0.001), 64 and 29% for **colonization factor antigen I** (P < 0.01), 53 and 21% for coli **surface antigen 2** (P < 0.05) and 58 and 4% for coli **surface antigen 4** (P < 0.001), respectively. The third vaccine dose was followed by augmented IgG antitoxin titers. CONCLUSION: The oral **enterotoxigenic** E. **coli** vaccine was safe and immunogenic in this setting in Egyptian infants.

L18 ANSWER 13 OF 39 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2001248081 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11292698
TITLE: Induction of systemic antifimbria and antitoxin antibody responses in Egyptian children and adults by an oral, killed **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B**

subunit vaccine.

AUTHOR: Hall E R; Wierzba T F; Ahren C; Rao M R; Bassily S; Francis W; Girgis F Y; Safwat M; Lee Y J; Svennerholm A M; Clemens J D; Savarino S J

CORPORATE SOURCE: U.S. Naval Medical Research Unit No. Three, Cairo, Egypt.

CONTRACT NUMBER: Y1-HD-0026-01 (NICHD)

SOURCE: Infection and immunity, (2001 May) 69 (5) 2853-7. Journal code: 0246127. ISSN: 0019-9567.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200105

ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010510

AB We assessed serologic responses to an oral, killed whole-cell **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B**-subunit (**ETEC**-rCTB) vaccine in 73 Egyptian adults, 105 schoolchildren, and 93 preschool children. Each subject received two doses of vaccine or placebo 2 weeks apart, giving blood before immunization and 7 days after each dose. Plasma antibodies to rCTB and four vaccine-shared colonization factors (CFs) were measured by enzyme-linked immunosorbent assay. Immunoglobulin A (IgA) antibodies to rCTB and **CFA/I** were measured in all subjects, and those against **CS1**, **CS2**, and **CS4** were measured in all children plus a subset of 33 adults. IgG antibodies to these five antigens were measured in a subset of 30 to 33 subjects in each cohort. Seroconversion was defined as a >2-fold increase in titer after vaccination. IgA and IgG seroconversion to rCTB was observed in 94 to 95% of adult vaccinees, with titer increases as robust as those previously reported for these two pediatric cohorts. The proportion showing IgA seroconversion to each CF antigen among vaccinated children (range, 70 to 96%) and adults (31 to 69%), as well as IgG seroconversion in children (44 to 75%) and adults (25 to 81%), was significantly higher than the corresponding proportion in placebo recipients, except for IgA responses to CS2 in adults. IgA anti-CF titers peaked after one dose in children, whereas in all age groups IgG antibodies rose incrementally after each dose. Independently, both preimmunization IgA titer and age were inversely related to the magnitude of IgA responses. In conclusion, serologic responses to the ETEC-rCTB vaccine may serve as practical immune outcome measures in future pediatric trials in areas where ETEC is endemic.

L18 ANSWER 14 OF 39 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 2001227148 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11238232

TITLE: Dose-dependent circulating immunoglobulin A antibody-secreting cell and serum antibody responses in Swedish volunteers to an oral inactivated **enterotoxigenic** Escherichia **coli** vaccine.

AUTHOR: Jertborn M; Ahren C; Svennerholm A M

CORPORATE SOURCE: Department of Medical Microbiology and Immunology, Goteborg University, Guldhegsgatan 10, 413 46 Goteborg, Sweden.. marianne.jertborn@microbio.gu.se

SOURCE: Clinical and diagnostic laboratory immunology, (2001 Mar) 8 (2) 424-8.
Journal code: 9421292. ISSN: 1071-412X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010611
Last Updated on STN: 20010611
Entered Medline: 20010607

AB The immunogenicity of different preparations of an oral inactivated **enterotoxigenic** Escherichia **coli** (**ETEC**) vaccine was evaluated in Swedish volunteers previously unexposed to **ETEC** infection. The vaccine preparations consisted of recombinant **cholera** toxin **B** subunit (**CTB**) and various amounts of formalin-killed whole bacteria expressing the most prevalent colonization factor antigens (CFAs). Significant immunoglobulin A (IgA) antibody-secreting cell (ASC) responses against **CTB** and the various CFA components were seen in a majority of volunteers after two doses of ETEC vaccine independent of the vaccine lot given. The IgA ASC responses against **CTB** were significantly higher after the second than after the first immunization, whereas the CFA-specific IgA ASC responses were almost comparable after the first and second doses of ETEC vaccine. Two immunizations with one-third of a full dose of CFA-ETEC bacteria induced lower frequencies of IgA ASC responses against all the different CFAs than two full vaccine doses, i.e., 63 versus 80% for **CFA/I**, 56 versus 70% for **CS1**, 31 versus 65% for **CS2**, and 56 versus 75% for **CS4**. The proportion of vaccinees responding with rises in the titer of serum IgA antibody against the various CFA antigens was also lower after immunization with the reduced dose of CFA-ETEC bacteria. These findings suggest that measurements of circulating IgA ASCs can be used not only for qualitative but also for quantitative assessments of the immunogenicity of individual fimbrial antigens in various preparations of ETEC vaccine.

L18 ANSWER 15 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:223217 BIOSIS
DOCUMENT NUMBER: PREV200200223217
TITLE: Construction of a multivalent Shigella-ETEC hybrid vaccine.
AUTHOR(S): Barry, E. [Reprint author]; Altboum, Z. [Reprint author]; Nijenhuis, T. [Reprint author]; Levine, M.
CORPORATE SOURCE: University of Maryland, Baltimore, Baltimore, MD, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 343-344. print.
Meeting Info.: 101st General Meeting of the American

Society for Microbiology. Orlando, FL, USA. May 20-24, 2001. American Society of Microbiology. ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Apr 2002
Last Updated on STN: 3 Apr 2002

AB Shigella spp. and **enterotoxigenic** Escherichia **coli** (**ETEC**) continue to be important causes of diarrheal disease in infants and young children in developing countries and are two major etiologic agents of traveler's diarrhea. Attenuated strains of Shigella have been developed as live, oral vaccines against shigellosis. Here, the attenuated strains of Shigella have been used as carriers of ETEC antigens to form a hybrid vaccine targeting common populations against two important pathogens. Protective immunity against ETEC is believed to be directed against fimbrial antigens of which there are multiple antigenically distinct types. Using the guaBA attenuated Shigella vaccine strain CVD 1204 as the vector, we have expressed four different ETEC fimbriae individually including **CFA/I**, **CS2**, **CS3**, and **CS4**. Following mucosal immunization in the guinea pig model serum IgG and mucosal IgA responses were elicited against each fimbriae. An additional strain was constructed expressing a detoxified version of **heat labile** toxin (LThK63). A mixed immunization experiment was performed to determine if immune responses could be elicited against multiple ETEC antigens and the Shigella vector itself and to determine if interference or diminution of responses would occur compared to individual antigens alone. Following mucosal immunization in the guinea pig model with an inoculum containing five Shigella strains each expressing a different ETEC antigen, immune responses against each antigen plus the Shigella vector were observed.

L18 ANSWER 16 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:201427 BIOSIS
DOCUMENT NUMBER: PREV200200201427
TITLE: Serum and mucosal immune responses measured against **CS6** and **CFA/I** colonization factors in an **enterotoxigenic** Escherichia **coli** murine intranasal model.
AUTHOR(S): Byrd, W. [Reprint author]; Cassels, F. [Reprint author]
CORPORATE SOURCE: Walter Reed Army Institute of Research, Silver Spring, MD, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 295. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology. Orlando, FL, USA. May 20-24, 2001. American Society for Microbiology. ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English
ENTRY DATE: Entered STN: 20 Mar 2002
Last Updated on STN: 20 Mar 2002

AB We have used the mouse intranasal (IN) model to measure the immunogenicity of encapsulated and unencapsulated colonization factors (CF) isolated from two strains of **enterotoxigenic** Escherichia **coli** (**ETEC**), strains B7A (**CS6**+) and H10407 (**CFA/I**+). The mice were immunized with either the encapsulated or native CF (**CS6** or **CFA/I**) (10 ug) with or without the nontoxic mutant form of the **heat-labile** enterotoxin (mLT) (5 ug) as an adjuvant. An ELISA was used to measure the titers of the antibody isotypes (IgG, IgA, and IgM) and IgG subclasses (IgG1, IgG2a, IgG2b, and IgG3) detected in serum and mucosal collections (saliva and fecal pellets) against the CF. Following the third vaccination, the serum CS6 IgG titers from the CS6 and CS6-encapsulated vaccinated mice were 1/12,800; however, when the mLT was administered simultaneously as an adjuvant the serum CS6 IgG titers rose to 1/102,400. No serum CS6 IgA or IgM from CS6 or CS6-encapsulated vaccinated mice were detected but when the mLT was administered along with these antigens serum CS6 IgA and IgM antibody titers were detected. The CS6 IgG and IgA titers measured in the fecal pellets were significantly higher in the mice administered CS6-mLT as compared to that from the mice administered CS6 alone. No CS6 IgG or IgA titers were detected in the saliva of the mice administered CS6 or CS6-encapsulated but were detected when the mLT was administered as an adjuvant simultaneously with these antigens. The serum CFA/I IgG, IgA, and IgM titers from CFA/I and CFA/I-mLT vaccinated mice were identical. The IgG subclass titers to **CS6** and **CFA/I** gave a mixed Th1/Th2 response with a significantly greater Th2 response (i.e., stimulated primarily an antibody response). The administration of the CF antigens IN to mice can be used to measure the antibody and Th1/Th2 responses to these ETEC antigens in serum and mucosal collections.

L18 ANSWER 17 OF 39 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2001464192 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11508385
TITLE: Toxins and colonization factor antigens of **enterotoxigenic** Escherichia **coli** among residents of Jakarta, Indonesia.
AUTHOR: Oyofo B A; Subekti D S; Svennerholm A M; Machpud N N; Tjaniadi P; Komalarini T S; Setiawan B; Campbell J R; Corwin A L; Lesmana M
CORPORATE SOURCE: United States Naval Medical Research Unit No. 2, Jakarta, Indonesia.
SOURCE: American journal of tropical medicine and hygiene, (2001 Aug) 65 (2) 120-4.
Journal code: 0370507. ISSN: 0002-9637.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20010910

Searcher : Shears 571-272-2528

Entered Medline: 20010906

AB Infection caused by **enterotoxigenic** Escherichia **coli** (**ETEC**) poses a serious health problem among children and adults in developing countries. Colonization of the small intestinal mucosa by ETEC strains is mediated by antigenically specific fimbriae, also known as colonization factor antigens (CFA). The significance of this study arises from reports that active and passive immunization with ETEC strains harboring CFAs has previously been shown to induce protective immunity against diarrhea in animal models. The aim of this study was to determine toxin-associated CFAs of ETEC isolated from a diarrheal disease case-control study in Jakarta, Indonesia. Thirteen hundred and twenty-three diarrheic and control patients with lactose-fermenting colonies were screened by ganglioside GM1-enzyme-linked immunosorbent assay (GM1-ELISA) for **heat-labile** (**LT**) and **heat-stable** (**ST**) **toxins**. Two hundred and forty-six (19%) ETEC isolates identified by GM1-ELISA for the **LT/ST toxins** were screened for CFAs by Dot blot assay using monoclonal antibodies against CFA/I, II, and IV and against the putative colonization antigens (PCF) PCFO159, PCFO166, CS7, and CS17. Of the 246 ETEC isolates, 177 (72%) elaborated **ST**, 56 (23%) produced **LT**, while 13 (5%) elicited both the **ST** and **LT toxins**. CFA testing of the 246 ETEC isolates showed that 21 (8%) expressed **CFA/I**, 3 (1%) exhibited **CFA/II**, 14 (6%) elaborated **CFA/IV**, while 7 (3%) expressed PCFO159 and PCFO159 plus **CS5**. No CFAs or PCFs could be associated with 201 (82%) of the ETEC strains. This report documents the types of CFAs associated with ETEC strains in Jakarta, Indonesia. These data may help current research efforts on the development of CFA-based vaccines for humans against ETEC and provide additional information for future ETEC vaccine trials in Southeast Asia.

L18 ANSWER 18 OF 39 TOXCENTER COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2001:92153 TOXCENTER
COPYRIGHT:	Copyright 2004 ACS
TITLE:	The Use of Attenuated Shigella Vaccine Strains to Deliver Heterologous Antigens and DNA Vaccines
AUTHOR(S):	Barry, Eileen M.; Altboum, Zeev; Anderson, Richard; Pasetti, Marcela; Levine, Myron M.
CORPORATE SOURCE:	Center for Vaccine Development, University of Maryland, Baltimore, MD, 21201, USA.
SOURCE:	Abstracts of Papers - American Chemical Society, (2001) Vol. 221st, pp. BIOT-046. CODEN: ACSRAL. ISSN: 0065-7727.
COUNTRY:	UNITED STATES
DOCUMENT TYPE:	Journal
FILE SEGMENT:	CAPLUS
OTHER SOURCE:	CAPLUS 2001:197353
LANGUAGE:	English
ENTRY DATE:	Entered STN: 20011116 Last Updated on STN: 20030401

AB Attenuated strains of Shigella have been developed as live oral vaccines against shigellosis. With further genetic manipulation these strains have been used to express heterologous antigens from

other pathogens and deliver these antigens to the host immune system. Attenuated S. flexneri strain CVD 1204 has been used to create a multivalent hybrid Shigella/**enterotoxigenic** E. **coli** (**ETEC**) vaccine. Expression plasmids have been constructed to allow the stable expression of four different ETEC fimbrial antigens including **CFA/I**, **CS2**, **CS3**, and **CS4** as well as detoxified **heat labile** toxin individually in CVD 1204. Addnl. constructions have been designed encoding multiple operons to direct expression of two antigens in a single Shigella strain. In a mucosal immunization model in guinea pigs, serum IgG and mucosal IgA responses were elicited against each ETEC antigen and the Shigella vector strain itself and immunized guinea pigs were protected against challenge with wild type Shigella. In addition, these strains have been investigated as an alternative method for the delivery of DNA vaccine plasmids to the host. In a model system, fragment C of tetanus toxin encoded on a eukaryotic expression plasmid was delivered by attenuated Shigella strain CVD 1204 to guinea pigs by mucosal immunization. The Shigella-delivered DNA vaccine was able to elicit anti-fragment C antibody titers comparable to those elicited by CVD 1204 expressing fragment C by a prokaryotic expression system as well as engendering protection against wild type Shigella challenge.

L18 ANSWER 19 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
DUPLICATE 12

ACCESSION NUMBER: 2000-442539 [38] WPIDS
DOC. NO. CPI: C2000-134660
TITLE: New oral vaccine against **enterotoxigenic** Escherichia **coli** which cause diarrhea comprising colonization factor antigens.
DERWENT CLASS: B04 D16
INVENTOR(S): ASKELOEF, P; BJARE, U; CARLIN, N; ASKELOF, P
PATENT ASSIGNEE(S): (SBLV-N) SBL VACCIN AB
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000037106	A1	20000629	(200038)*	EN	11
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
SE 9804415	A	20000619	(200042)		
AU 2000030889	A	20000712	(200048)		
SE 515285	C2	20010709	(200141)		
NO 2001002889	A	20010612	(200157)		
BR 9916278	A	20010904	(200160)		
EP 1140159	A1	20011010	(200167)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
Z 2001001947	A3	20011212	(200206)		
N 1330552	A	20020109	(200229)		

Searcher : Shears 571-272-2528

KR 2001101233	A	20011114	(200230)	
ZA 2001004362	A	20020327	(200230)	15
HU 2001004552	A2	20020429	(200238)	
JP 2002532562	W	20021002	(200279)	15
MX 2001006200	A1	20020501	(200368)	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000037106	A1	WO 1999-SE2306	19991209
SE 9804415	A	SE 1998-4415	19981218
AU 2000030889	A	AU 2000-30889	19991209
SE 515285	C2	SE 1998-4415	19981218
NO 2001002889	A	WO 1999-SE2306	19991209
		NO 2001-2889	20010612
BR 9916278	A	BR 1999-16278	19991209
		WO 1999-SE2306	19991209
EP 1140159	A1	EP 1999-964847	19991209
		WO 1999-SE2306	19991209
CZ 2001001947	A3	WO 1999-SE2306	19991209
		CZ 2001-1947	19991209
CN 1330552	A	CN 1999-814553	19991209
KR 2001101233	A	KR 2001-707484	20010615
ZA 2001004362	A	ZA 2001-4362	20010528
HU 2001004552	A2	WO 1999-SE2306	19991209
		HU 2001-4552	19991209
JP 2002532562	W	WO 1999-SE2306	19991209
		JP 2000-589216	19991209
MX 2001006200	A1	WO 1999-SE2306	19991209
		MX 2001-6200	20010618

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000030889	A	Based on	WO 2000037106
BR 9916278	A	Based on	WO 2000037106
EP 1140159	A1	Based on	WO 2000037106
CZ 2001001947	A3	Based on	WO 2000037106
HU 2001004552	A2	Based on	WO 2000037106
JP 2002532562	W	Based on	WO 2000037106
MX 2001006200	A1	Based on	WO 2000037106

PRIORITY APPLN. INFO: SE 1998-4415 19981218

AN 2000-442539 [38] WPIDS

AB WO 200037106 A UPAB: 20000811

NOVELTY - New oral vaccine (I) against **enterotoxigenic** Escherichia **coli** causing diarrhea in humans is new and comprises a defined amount of at least three types of colonization factor antigens on killed E. coli bacteria lacking the gene encoding the **heat labile** (**LT**) **enterotoxin** with the **B**-subunit of **cholera toxin** (**CTB**) and a vehicle.

DETAILED DESCRIPTION - New oral vaccine (I) against **enterotoxigenic** Escherichia **coli** causing diarrhea

in humans is new and comprises a defined amount of at least three types of colonization factor antigens (CFAs) e.g. **CFA I, CFA II** (**CS 1** and **CS 2** and **CS 3**) and **CFA IV** (**CS 4, CS 5** and **CS 6**), on killed E. coli bacteria lacking the gene encoding the **heat labile** (**LT**) **enterotoxin**, together with a predefined amount of the **B**-subunit of **cholera toxin** (**CTB**) and a vehicle, which vaccine composition is purified from possible **heat stable enterotoxin**.

ACTIVITY - Antibacterial; Antidiarrheic.

MECHANISM OF ACTION - Vaccine.

Formulations were given to 3 randomized groups of travelers: (1) 1 mg recombinant **B**-subunit of **cholera** toxin plus 1011 formalin killed ETEC bacteria of five ETEC strains expressing the most common colonization factor antigens; (2) a **B**-subunit **cholera** whole cell vaccine containing 1 mg recombinant subunit **B cholera** toxin and 1011 killed whole cells; and (3) placebo containing 1011 killed E. coli K12. The formulations were suspended in 4 ml buffer and each dose of vaccine or placebo was given as a drink in 150 cc of a sodium hydrogen carbonate solution. 250 volunteers received one dose of vaccine or placebo of whom 246 also received a second dose. 43 volunteers (17%) had mild to moderate gastrointestinal or general symptoms, 13 (16%) in the placebo, 13 (16%) in the cholera vaccine group and 17 (20%) in the ETEC vaccine group. After the second dose 20 (8%) had symptoms, 6 (7%) in the placebo, 7 (9%) in the cholera vaccine group and 7 (8%) in the ETEC vaccine group.

USE - The oral vaccine is useful against diarrhea, especially against **enterotoxigenic** Escherichia **coli** causing diarrhea in humans.

Dwg.0/0

L18 ANSWER 20 OF 39 MEDLINE on STN DUPLICATE 13

ACCESSION NUMBER: 2000404315 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10899847

TITLE: Safety and immunogenicity of two different lots of the oral, killed **enterotoxigenic** escherichia **coli-cholera** toxin **B** subunit vaccine in Israeli young adults.

AUTHOR: Cohen D; Orr N; Haim M; Ashkenazi S; Robin G; Green M S; Ephros M; Sela T; Slepon R; Ashkenazi I; Taylor D N; Svennerholm A M; Eldad A; Shemer J

CORPORATE SOURCE: Army Health Branch Research Unit, Medical Corps, Israel Defence Force, Israel.. danic@netvision.net.il

SOURCE: Infection and immunity, (2000 Aug) 68 (8) 4492-7. Journal code: 0246127. ISSN: 0019-9567.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

GMENT: Priority Journals

ONTH: 200008

Searcher : Shears 571-272-2528

ENTRY DATE: Entered STN: 20000901
Last Updated on STN: 20000901
Entered Medline: 20000824

AB **Enterotoxigenic** Escherichia **coli** (**ETEC**) is one of the leading causes of diarrhea among Israeli soldiers serving in field units. Two double-blind placebo-controlled, randomized trials were performed among 155 healthy volunteers to evaluate the safety and immunogenicity of different lots of the oral, killed ETEC vaccine consisting of two doses of whole cells plus recombinantly produced **cholera** toxin **B** subunit (rCTB). The two doses of vaccine lot E005 and the first dose of vaccine lot E003 were well tolerated by the volunteers. However, 5 (17%) vaccinees reported an episode of vomiting a few hours after the second dose of lot E003; none of the placebo recipients reported similar symptoms. Both lots of vaccine stimulated a rate of significant antibody-secreting cell (ASC) response to **CTB** and to colonization factor antigen I (CFA/I) after one or two doses, ranging from 85 to 100% and from 81 to 100%, respectively. The rate of ASC response to **CS2**, **CS4**, and **CS5** was slightly lower than the rate of ASC response induced to **CTB**, **CFA/I**, and **CS1**. The second vaccine dose enhanced the response to **CTB** but did not increase the frequencies or magnitude of ASC responses to the other antigens. The two lots of the ETEC vaccine induced similar rates of serum antibody responses to **CTB** and CFA/I which were less frequent than the ASC responses to the same antigens. Based on these safety and immunogenicity data, an efficacy study of the ETEC vaccine is under way in the Israel Defense Force.

L18 ANSWER 21 OF 39 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 2000085104 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10618058
TITLE: Prevalence of toxin types and colonization factors in **enterotoxigenic** Escherichia **coli** isolated during a 2-year period from diarrheal patients in Bangladesh.
AUTHOR: Qadri F; Das S K; Faruque A S; Fuchs G J; Albert M J; Sack R B; Svennerholm A M
CORPORATE SOURCE: International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka 1000, Bangladesh.. fqadri@icddrb.org
SOURCE: Journal of clinical microbiology, (2000 Jan) 38 (1) 27-31.
Journal code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000229
Last Updated on STN: 20000229
Entered Medline: 20000217

AB The prevalence of toxin types and colonization factors (CFs) of **enterotoxigenic** Escherichia **coli** (**ETEC**) was prospectively studied with fresh samples (n = 4,662) obtained

from a 2% routine surveillance of diarrheal stool samples over 2 years, from September 1996 to August 1998. Stool samples were tested by enzyme-linked immunoassay techniques and with specific monoclonal antibodies for the toxins and CFs. The prevalence of ETEC was 14% (n = 662), with over 70% of the strains isolated from children 0 to 5 years of age, of whom 93% were in the 0- to 3-year-old age range. Of the total ETEC isolates, 49.4% were positive for the **heat-stable toxin** (**ST**), 25.4% were positive for the **heat-labile toxin** (**LT**) only, and 25.2% were positive for both **LT** and **ST**. The rate of ETEC isolation peaked in the hot summer months of May to September and decreased in winter. About 56% of the samples were positive for 1 or more of the 12 CFs that were screened for. The coli surface antigens **CS4**, **CS5**, and/or **CS6** of the **colonization factor antigen** (**CFA**)/**IV** complex were most prevalent (incidence, 31%), followed by **CFA/I** (23.5%) and coli surface antigens **CS1**, **CS2**, and **CS3** of **CFA/II** (21%). In addition, other CFs detected in decreasing order were CS7 (8%), CS14 (PCFO166) (7%), CS12 (PCFO159) (4%), CS17 (3%), and CS8 (CFA/III) (2.7%). The ST- or LT- and ST-positive ETEC isolates expressed the CFs known to be the most prevalent (i.e., CFA/I, CFA/II, and CFA/IV), while the strains positive for LT only did not. Among children who were infected with ETEC as the single pathogen, a trend of relatively more severe disease in children infected with ST-positive ($P < 0.001$) or LT- and ST-positive ($P < 0.001$) ETEC isolates compared to the severity of the disease in children infected with LT only-positive ETEC isolates was seen. This study supports the fact that ETEC is still a major cause of childhood diarrhea in Bangladesh, especially in children up to 3 years of age, and that measures to prevent such infections are needed in developing countries.

L18 ANSWER 22 OF 39 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-458391 [38] WPIDS
DOC. NO. CPI: C1999-134579
TITLE: Preparation of time and temperature cross-linked vaccine delivering immunogenic components to the mucosal immune system.
DERWENT CLASS: B04 D16
INVENTOR(S): EWALT, K L; HANDLEY, H H
PATENT ASSIGNEE(S): (MAXI-N) MAXIM PHARM INC
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9936088	A1	19990722	(199938)*	EN	61
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9922323	A	19990802	(199954)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9936088	A1	WO 1999-US943	19990115
AU 9922323	A	AU 1999-22323	19990115

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9922323	A	Based on	WO 9936088

PRIORITY APPLN. INFO: US 1998-71607P 19980116
AN 1999-458391 [38] WPIDS
AB WO 9936088 A UPAB: 19990922
NOVELTY - Making a time and temperature cross-linked vaccine preparation comprises cross-linking an immunogenic component and carrier component for at least two weeks at no more than 15 deg. C.

DETAILED DESCRIPTION - Making a time and temperature cross-linked vaccine preparation comprises cross-linking an immunogenic component and carrier component for at least two weeks at no more than 15 deg. C.

An INDEPENDENT CLAIM is also included for a vaccine prepared by the above method.

USE - For delivering immunogenic components to the mucosal immune system. Targets for the vaccine are organisms which cause a variety of conditions such as sexually transmitted diseases, pulmonary, intestinal, lacrimal and aural infections (such as HIV, hepatitis B and gonorrhea), sexually transmitted cancer associated viruses (such as human papilloma virus), influenza virus, tuberculosis, diphtheria, rubella, H.pylori and Lyme's disease.

ADVANTAGE - The vaccine produces a long lasting protective mucosal and systemic immunity to a variety of pathogens.
Dwg.0/18

L18 ANSWER 23 OF 39 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 15
ACCESSION NUMBER: 1999266491 EMBASE
TITLE: Characterization of an **enterotoxigenic** Escherichia **coli** strain from Africa expressing a putative colonization factor.
AUTHOR: Khalil S.B.; Cassel F.J.; Shaheen H.I.; Pannell L.K.; El-Ghorab N.; Kamal K.; Mansour M.; Savarino S.J.; Peruski L.F. Jr.
CORPORATE SOURCE: L.F. Peruski Jr., c/o Commanding Officer, U.S. Naval Medical Res. Unit No. 3, PSC 452, FPO AE 09835-0007, United States. boushrah@namru3.navy.mil
SOURCE: Infection and Immunity, (1999) 67/8 (4019-4026).
Refs: 46
ISSN: 0019-9567 CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English

Searcher : Shears 571-272-2528

SUMMARY LANGUAGE: English

AB An **enterotoxigenic** Escherichia **coli** (**ETEC**) strain of serotype O114:H- that expressed both **heat-labile** and **heat-stable** enterotoxins and tested negative for colonization factors (CF) was isolated from a child with diarrhea in Egypt. This strain, WS0115A, induced hemagglutination of bovine erythrocytes and adhered to the enterocyte-like cell line Caco-2, suggesting that it may elaborate novel fimbriae. Surface-expressed antigen purified by differential ammonium sulfate precipitation and column chromatography yielded a single protein band with M(r) 14,800 when resolved by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (16% polyacrylamide). A monoclonal antibody against this putative fimbrial antigen was generated and reacted with strain WS0115A and also with **CS1**-, CS17-, and CS19-positive strains in a dot blot assay. Reactivity was temperature dependent, with cells displaying reactivity when grown at 37δC but not when grown at 22δC. Immunoblot analysis of a fimbrial preparation from strain WS0115A showed that the monoclonal antibody reacted with a single protein band. Electron microscopy and immunoelectron microscopy revealed fimbria-like structures on the surface of strain WS0115A. These structures were rigid and measured 6.8 to 7.4 nm in diameter. Electrospray mass-spectrometric analysis showed that the mass of the purified fimbria was 14,965. Da. The N-terminal sequence of the fimbria established that it was a member of the **CFA/I** family, with sequence identity to the amino terminus of CS19, a new CF recently identified in India. Cumulatively, our results suggest that this fimbria is CS19. Screening of a collection of **ETEC** strains isolated from children with diarrhea in Egypt found that 4.2% of strains originally reported as CF negative were positive for this CF, suggesting that it is biologically relevant in the pathogenesis of **ETEC**.

L18 ANSWER 24 OF 39 MEDLINE on STN DUPLICATE 16

ACCESSION NUMBER: 1999059858 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9841829

TITLE: Oral, inactivated, whole cell **enterotoxigenic** Escherichia **coli** plus **cholera** toxin **B** subunit vaccine: results of the initial evaluation in children. PRIDE Study Group.

AUTHOR: Savarino S J; Hall E R; Bassily S; Brown F M; Youssef F; Wierzba T F; Peruski L; El-Masry N A; Safwat M; Rao M; El Mohamady H; Abu-Elyazeed R; Naficy A; Svennerholm A M; Jertborn M; Lee Y J; Clemens J D

CORPORATE SOURCE: US Naval Medical Research Unit Number 3, Bethesda, MD, USA.. savarino@namru3.navy.mil

CONTRACT NUMBER: HD-0026-01 (NICHD)
SOURCE: Journal of infectious diseases, (1999 Jan) 179 (1) 107-14.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990203

AB Two randomized, double-blinded trials assessed the safety and immunogenicity of an oral, killed **enterotoxigenic** Escherichia **coli** (**ETEC**) plus **cholera** toxin **B** subunit vaccine in Egyptian children. Two doses of vaccine or E. coli K-12 were given 2 weeks apart to 105 6- to 12-year-olds and 97 2- to 5-year-olds. Safety was monitored for 3 days after each dose. Blood was collected before immunization and 7 days after each dose to measure immune responses. Few children reported postdosing symptoms, with no differences in the frequency of symptoms between treatment groups. Most vaccinees had an IgA antibody-secreting cell response against **colonization factor antigen I** (100%, 6-12 years; 95%, 2-5 years), coli **surface antigen 2** (92%, 6-12 years; 83%, 2-5 years), and coli **surface antigen 4** (93%, 6-12 years). Vaccination evoked a >/=4-fold rise in antitoxic IgA and IgG titers in 93% and 81% of children, respectively. In conclusion, the oral ETEC vaccine was safe and immunogenic in 2- to 12-year-old children, justifying further evaluation in infants.

L18 ANSWER 25 OF 39 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 1998158233 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9498468
TITLE: Safety and immunogenicity of an oral, killed **enterotoxigenic** Escherichia **coli-cholera** toxin **B** subunit vaccine in Egyptian adults.
AUTHOR: Savarino S J; Brown F M; Hall E; Bassily S; Youssef F; Wierzba T; Peruski L; El-Masry N A; Safwat M; Rao M; Jertborn M; Svennerholm A M; Lee Y J; Clemens J D
CORPORATE SOURCE: US Naval Medical Research Unit No. 3, Cairo, Egypt.. savarino@namru3.navy.mil
CONTRACT NUMBER: HD-0026-01 (NICHD)
SOURCE: Journal of infectious diseases, (1998 Mar) 177 (3) 796-9.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980407
Last Updated on STN: 19980407
Entered Medline: 19980326

AB **Enterotoxigenic** Escherichia **coli** (**ETEC**) is the leading cause of bacterial diarrhea in young children in developing countries. The safety and immunogenicity of a killed, oral ETEC vaccine consisting of whole cells plus recombinantly produced **cholera** toxin **B** subunit (rCTB) was evaluated in Egypt, which is endemic for ETEC diarrhea.

Seventy-four healthy Egyptian adults (21-45 years old) were randomized and received two doses of the ETEC/rCTB vaccine (E003) or placebo 2 weeks apart. The frequency of adverse events after either dose did not differ by treatment group, and no severe adverse events were reported. After vaccination, peripheral blood IgA B cell responses to **CTB** (100%) and to vaccine **colonization factor antigens CFA /I** (94%), **CS4** (100%), **CS2** (81%), and **CS1** (69%) were significantly higher than response rates for the placebo group. These favorable results in Egyptian adults indicate that the ETEC/rCTB vaccine is a promising candidate for evaluation in younger age groups in this setting.

L18 ANSWER 26 OF 39 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 1998269922 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9607039
TITLE: Safety and immunogenicity of an oral inactivated **enterotoxigenic** Escherichia **coli** vaccine.
AUTHOR: Jertborn M; Ahren C; Holmgren J; Svennerholm A M
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, Goteborg University, Sweden.
SOURCE: Vaccine, (1998 Jan-Feb) 16 (2-3) 255-60.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980713
Last Updated on STN: 19980713
Entered Medline: 19980629

AB The safety and immunogenicity of two different lots, 001 and 003, of an oral inactivated **enterotoxigenic** Escherichia **coli** (**ETEC**) vaccine consisting of a mixture of formalin-killed whole bacteria expressing the most prevalent colonisation factor antigens, i.e. CFA/I, CFA/II and CFA/IV and recombinantly produced **cholera B** subunit (rCTB) have been evaluated in Swedish volunteers. Neither of the two vaccine preparations, containing different CFA/II-expressing strains but otherwise identical, gave rise to any significant side-effects. Mucosal immune responses, as reflected in antibody-secreting cell (ASC) responses in peripheral blood, were studied after two doses of vaccine and did not differ significantly for the two vaccine lots. Vaccination induced high levels of **CTB**-specific IgA ASCs in 100% of the volunteers, and significant IgA ASC responses (9- to 36-fold) were noted in 84% of them against **CFA/I** , in 87% against **CFA/II** subcomponents **CS1**-**CS3** and in 91% against **CFA/ IV** subfactors **CS4** and/or **CS5**. The frequencies and magnitudes of CFA IgA ASC responses were similar when giving the vaccine with a 1 or 2 week interval. Results from serological analyses showed that the local IgA responses against CFAs are only infrequently associated with serum antibody titre rises.

L18 ANSWER 27 OF 39 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 1998418525 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9747753
TITLE: Epidemiology and properties of **heat-stable enterotoxin**-producing Escherichia **coli** serotype O169:H41.
AUTHOR: Nishikawa Y; Helander A; Ogasawara J; Moyer N P; Hanaoka M; Hase A; Yasukawa A
CORPORATE SOURCE: Department of Epidemiology, Osaka City Institute of Public Health and Environmental Sciences, Tennoji, Osaka, Japan.
SOURCE: Epidemiology and infection, (1998 Aug) 121 (1) 31-42. Journal code: 8703737. ISSN: 0950-2688.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19981008
Last Updated on STN: 19981008
Entered Medline: 19980929

AB **Enterotoxigenic** Escherichia **coli** (**ETEC**) serotype O169:H41 organisms have become the most prevalent **ETEC** in Japan since the first outbreak in 1991. It was assumed that the outbreaks were due to clonal spread of this new ETEC serotype. The relationship of 32 strains isolated from 6 outbreaks were examined for biotype, antibiotic susceptibility, enterotoxigenicity, protein banding pattern, lipopolysaccharide banding pattern, plasmid analysis, and ribotyping. Further, the strains were examined by haemagglutination, surface hydrophobicity, and the ability to adhere to HEp-2 cells. The present study suggests that the outbreaks were caused by multiple clones of STp-producing O169:H41 since they showed differences in ribotype and outer membrane protein banding patterns. The strains did not agglutinate human or bovine red blood cells in a mannose-resistant manner. They adhered to HEp-2 cells in a manner resembling enteroaggregative E. coli. Five strains were examined by dot-blot tests for the **colonization factor antigens CFA/I, CS1, CS2, CS3, CS4, CS5, CS6**, CS7, PCFO159, PCFO166 and CFA/III. Although four strains expressed CS6, no structure for CS6 was identified. A strain that the anti-CS6 MAbs did not react with could adhere to HEp-2 cells in mannose resistant manner; thus, it is unlikely that CS6 play an important role in the adhesion to the cells. Electron microscopy studies of the O169:H41 strains suggested that curly fimbriae, a possible new colonization factor, may be playing an important role in the adhesion of the bacteria to HEp-2 cells. In conclusion, outbreaks due to ETEC O169:H41 were caused by multiple clones, and the strains should be examined in detail for a possible new colonization factor.

L18 ANSWER 28 OF 39 MEDLINE on STN DUPLICATE 20
ACCESSION NUMBER: 1998020877 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9382733
TITLE: Epitope analysis of the CS3 fimbrial subunit of human

enterotoxigenic Escherichia **coli** and the construction of novel CS3::ST and CS3::LT-B immunogens.

AUTHOR: Yakhchali B; Manning P A
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Adelaide, Australia.

SOURCE: Behring Institute Mitteilungen, (1997 Feb) (98) 124-34.
Journal code: 0367532. ISSN: 0301-0457.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971110

AB **Enterotoxigenic** E. **coli** (**ETEC**) are the major cause of traveler's diarrhoea and the **CS3** fimbriae/fibrillae are expressed by most strains bearing the colonization factor **CFA/II**. The cstAH gene cluster determining CS3 biosynthesis has been previously cloned and sequenced and it has been shown that cstH encodes the major fimbrial subunit and cstA-G encode an assembly cassette. In the work described here we have sought to define the surface exposed domains on CS3 and to manipulate them so that CS3 can be used as a means of expressing foreign antigenic determinants on the bacterial surface. Using a panel of 21 monoclonal antibodies, which we have used in western blotting, immunofluorescence microscopy and colony blotting, together with computer predictions, we have identified three domains within CstH. Two of these sites were permissive for insertion and we have introduced, in-frame, either an epitope from the B subunit of **LT** (**heat labile toxin**) or the entire coding sequence of mature **ST** (**heat stable toxin**) to construct hybrid proteins. These proteins could be assembled into hybrid fimbriae which could be recognized by antibodies to both CS3 and the foreign epitope as shown by immunofluorescence microscopy and colony blotting. The immunogenicity of the constructs has been evaluated following both oral and intraperitoneal immunization of mice with the attenuated Salmonella typhimurium strain G30 harbouring the hybrid cst operons. Although plasmid stability is currently a problem, these experiments showed that antibodies to both the carrier and the foreign epitope were generated.

L18 ANSWER 29 OF 39 MEDLINE on STN DUPLICATE 21
ACCESSION NUMBER: 96178643 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8606115
TITLE: Detection of the enteroaggregative Escherichia **coli heat-stable enterotoxin** 1 gene sequences in **enterotoxigenic** E. **coli** strains pathogenic for humans.
AUTHOR: Yamamoto T; Echeverria P
CORPORATE SOURCE: Department of Infectious Diseases and Tropical Medicine, Research Institute, International Medical

Center of Japan, Tokyo.
SOURCE: Infection and immunity, (1996 Apr) 64 (4) 1441-5.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-S81691
ENTRY MONTH: 199605
ENTRY DATE: Entered STN: 19960531
Last Updated on STN: 19980206
Entered Medline: 19960523

AB The sequence of the enteroaggregative Escherichia **coli enterotoxin** 1 (EAST1) gene was present in most (or all) strains of human-colonizing **enterotoxigenic** E. **coli** (**ETEC**) with **colonization factor antigen II** (**CFA/II**) or **CFA/IV** (**CS6**). The EAST1 gene was also strongly associated with PCF09+ ETEC or CFA/I+ ETEC elaborating heat-liable enterotoxin (and **heat-stable** enterotoxin I). In contrast, CFA/I+ ETEC elaborating **heat-stable** enterotoxin I, CFA/III+ ETEC, or CS17+ ETEC exhibited very weak or no associated. E. coli from healthy volunteers had no EAST1 gene sequence. A CFA/I+ ETEC strain (H10407) possessed multiple copies of the EAST1 gene on the CFA/I-encoding plasmid and chromosome. In one CFA/II+ ETEC strain, the EAST1 gene was present on the CFA/II-encoding plasmid. The EAST1 gene sequences of the CFA/I+ and CFA/II+ **ETEC** strains were identical to each other and 99.1% homologous to the reported gene sequence of enteroaggregative E. **coli**. The data indicate that the EAST1 gene is distributed among ETEC strains with a case of the presence of multiple copies in a single cell and that this distribution is associated with the adherence factor type.

L18 ANSWER 30 OF 39 MEDLINE on STN DUPLICATE 22
ACCESSION NUMBER: 96151480 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8564370
TITLE: Colonization factors of **enterotoxigenic** E. **coli** (**ETEC**) from residents of northern Egypt.
AUTHOR: Oyofo B A; el-Etr S H; Wasfy M O; Peruski L; Kay B; Mansour M; Campbell J R; Svennerholm A M; Churilla A M; Murphy J R
CORPORATE SOURCE: U.S. Naval Medical Research Unit No. 3, Cairo, Egypt.
SOURCE: Microbiological research, (1995 Nov) 150 (4) 429-36.
Journal code: 9437794. ISSN: 0944-5013.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960315
Last Updated on STN: 19960315
Entered Medline: 19960306

AB Infection caused by **enterotoxigenic** Escherichia **coli** (**ETEC**) poses a serious health problem to

children in developing countries. Colonization of the small intestinal mucosa by ETEC strains is mediated by antigenically specific fimbriae, also known as colonization factor antigens (CFA). The importance of this study arises from reports that active and passive immunization with ETEC strains harboring CFAs induced protective immunity against diarrhea in animal models with preformed antibodies. In humans, ETEC containing CFA/I, II, III and IV have been identified. The aim of this study was to define CFAs of ETEC isolated in Alexandria, Egypt. One hundred and seven ETEC isolates from 132 human residents in Alexandria, Egypt were isolated during a birth cohort study. ETEC isolates were screened for **heat labile** (**LT**) and **heat stable** (**ST**) **toxins** using a 32P oligonucleotide hybridization probe and a GM1 ELISA. These isolates were examined using monoclonal antibodies against CFA/I, II, III, IV, and against the putative colonization antigens PCF0159 and PCF0166, CS 7 and CS 17. CFAs were found in 48% of ETEC strains. CFA/I was found in 18% of the strains, CFA/II in 10% and CFA/IV in 14%. CFA III was not found. All fifteen strains expressing **CFA/IV** expressed **CS6** and produced ST. CFA/IV was not found in non-ST producing strains, while CFA/I was absent in ST-only producing strains.

L18 ANSWER 31 OF 39 MEDLINE on STN DUPLICATE 23
ACCESSION NUMBER: 95157343 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7854210
TITLE: Prevalence of colonization factor antigens (CFAs) and adherence to HeLa cells in **enterotoxigenic** Escherichia **coli** isolated from feces of children in Sao Paulo.
AUTHOR: Guth B E; Aguiar E G; Griffin P M; Ramos S R; Gomes T A
CORPORATE SOURCE: Department of Microbiology, Immunology and Parasitology, Escola Paulista de Medicina, Sao Paulo, Brazil.
SOURCE: Microbiology and immunology, (1994) 38 (9) 695-701. Journal code: 7703966. ISSN: 0385-5600.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950322
Last Updated on STN: 19970203
Entered Medline: 19950315

AB Fifty-eight **enterotoxigenic** Escherichia **coli** (**ETEC**) strains, isolated from children with and without diarrhea in Sao Paulo, were examined for the presence of colonization factor antigens (CFAs) and their ability to adhere to HeLa cells. Antisera to **CFA/I**, the coli surface (CS) antigens CS1CS3, CS2CS3, and **CS2** of **CFA/II**, CFA/III, and CS5CS6 and **CS6** of **CFA/IV** were used. CFAs were identified in 43% of the ETEC strains: 40% of the CFAs strains with **CFAs** harbored **CFA/I**, 24% carried **CFA/II** (CS1CS3), 24% carried **CFA/IV** (**CS6**),

and 12% carried **CFA/IV** (CS5CS6). CFAs occurred mainly among ETEC strains producing only **heat-stable** (**ST**-I) **enterotoxin** and in strains also producing **heat-labile toxin** (**LT**-I). No ETEC strains tested expressed CFA/III. A marked change in serotypes of ST-I-producing strains was found in Sao Paulo between 1979 and 1990. Adherence to HeLa cells was detected in 14% of the ETEC strains. All of them had a diffuse adherence pattern and produced only ST-I, and 88% carried CS6 antigen.

L18 ANSWER 32 OF 39 MEDLINE on STN DUPLICATE 24
ACCESSION NUMBER: 93390296 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1308901
TITLE: Relationship between **enterotoxigenic** Escherichia **coli** and diarrhea among children in Buenos Aires.
AUTHOR: Binsztein N; Rivas M; Lopez Moral L; Viboud G; Iriarte C; Szefner M; Svennerholm A M
CORPORATE SOURCE: Instituto Nacional de Microbiologia Carlos G. Malbran, Buenos Aires, Argentina.
SOURCE: Medicina, (1992) 52 (2) 103-8.
Journal code: 0204271. ISSN: 0025-7680.
PUB. COUNTRY: Argentina
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19931105
Last Updated on STN: 19931105
Entered Medline: 19931021

AB The incidence of **enterotoxigenic** Escherichia **coli** (**ETEC**) has been studied in 85 children with acute diarrhea in patients in the Hospital de Ninos Pedro de Elizalde, Buenos Aires, and in 38 healthy children. All of them were up to four years old and none had received antibiotic treatment within 7 days before sampling. ETEC was recovered in 9 out of 85 (10.6%) children with diarrhea. From these positive cases, 6 were associated with **heat-stable** (**ST**), 1 with **heat-labile** (**LT**) and 2 with both **LT** and **ST enterotoxins**. Only one case (2.6%) of LT-producing ETEC was detected in the control group. In 5 out of 9 ETEC diarrhea cases (55.5%) the isolated strains expressed human colonization factor antigens (CFA); four of them were CFA/I and one CFA/II. The characteristics of the CFA, biotype, serotype and antibiotic sensitivity pattern were studied in 23 E. **coli** isolates from 10 **ETEC** positive children. Of the 12 ST only strains, 5 (41.7%) expressed **CFA/I** and **2** (16.7%) **CFA/II** (**CS2** + **CS3**). One out of 2 LT/ST strains expressed CFA/I. CFAs were not detected in the **ETEC-LT** nor in the **toxin** negative E. **coli** strains. From the **ETEC** isolated, 82.4% were resistant to 4 or more antibiotics, whereas only 50% of simultaneously isolated toxin-negative E. **coli** presented this sensitivity pattern. The different ETEC strains belonged to several different serotypes, some of them rarely observed in other countries. None of these

serotypes correlated either with the toxin profile or with the sugar fermentation pattern.(ABSTRACT TRUNCATED AT 250 WORDS)

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ACCESSION NUMBER: 91242764 EMBASE
DOCUMENT NUMBER: 1991242764
TITLE: Positive regulation of **colonization factor antigen I** (**CFA/I**) production by **enterotoxigenic** Escherichia **coli** producing the colonization factors **CS5**, **CS6**, CS7, CS17, PCFO9, PCFO159:H4 and PCFO166.
AUTHOR: Hibberd M.L.; McConnell M.M.; Willshaw G.A.; Smith H.R.; Rowe B.
CORPORATE SOURCE: Division of Enteric Pathogens, Central Public Health Lab., 61 Colindale Avenue,London NW9 5HT, United Kingdom
SOURCE: Journal of General Microbiology, (1991) 137/8 (1963-1970).
ISSN: 0022-1287 CODEN: JGMIAN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Enterotoxigenic** Escherichia **coli** (**ETEC**) strains of nineteen serogroups which produced colonization factors (**coli**-surface-associated antigens **CS5**, **CS6**, CS7 and CS17, colonization factor antigen CFA/III and putative colonization factors PCFO159:H4, PCFO166 and PCFO9) were tested for hybridization with a DNA probe containing the cfaD sequence that regulates expression of **CFA/I**. Strong colony hybridization, similar to that with the **CFA/I**-positive control strain H10407, occurred with **ETEC** strains of serogroups O27, O159 and O169 which produced **CS6** antigen, and with all the strains which produced PCFO166 fimbriae. Weak colony hybridization, compared to the control strain, was found with **ETEC** producing **CS5** fimbriae with **CS6** antigen, CFA/III fimbriae with **CS6** antigen, CS7 fimbriae or PCFO159:H4 fimbriae. **CS6**-antigen-positive strains of serogroups O79, O89 and O148 and all the CS17-antigen-positive and PCFO9-fimbriae-positive strains were negative in colony hybridization tests with the cfaD probe. Plasmid DNA of nine **ETEC** strains and their colonization-factor-negative derivatives was tested for hybridization with the cfaD probe and with **ST** and **LT** oligonucleotide probes. The sequences that hybridized with the cfaD probe were on the plasmids which coded for **enterotoxin** production. Fifteen strains were transformed with NTP513, a recombinant plasmid which contains the **CFA/I** region **1** fimbrial subunit operon but lacks a functional cfaD sequence, in order to determine whether DNA in any of these strains could substitute for the cfaD sequence in the regulation of production of **CFA/I** fimbriae. Transformants of five strains which produced the

colonization factors **CS6**, PCFO166, **CS5** + **CS6**, CS7 and PCFO9, and of one strain which was a colonization-factor-negative derivative of the **CS5**, **CS6**-producing strain E17018, gave good production of **CFA/I** fimbriae comparable to the **CFA/I**-positive control strain H10407. Transformants of two strains, producing PCFO159 fimbriae and CS17 antigen, respectively, gave weak **CFA/I** production. Transformants of one strain producing **CS6** antigen and of six colonization-factor-negative derivatives did not produce **CFA/I** fimbriae. These results showed that plasmids in seven of eight types of colonization-factor-positive strains contained gene sequences which could substitute functionally for the cfaD sequence. Only two of these strains had gene sequences that hybridized strongly with the cfaD probe.

L18 ANSWER 34 OF 39 MEDLINE on STN DUPLICATE 25
ACCESSION NUMBER: 92129593 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1774313
TITLE: Colonization factors of **enterotoxigenic** Escherichia **coli** isolated from children with diarrhea in Argentina.
AUTHOR: Binsztein N; Jouve M J; Viboud G I; Lopez Moral L; Rivas M; Orskov I; Ahren C; Svennerholm A M
CORPORATE SOURCE: Instituto Nacional de Microbiologia Carlos G. Malbran, Buenos Aires, Argentina.
SOURCE: Journal of clinical microbiology, (1991 Sep) 29 (9) 1893-8.
Journal code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920322
Last Updated on STN: 19920322
Entered Medline: 19920303

AB A prospective study was performed to evaluate the presence of colonization factor antigens (CFAs) in **enterotoxigenic** Escherichia **coli** (**ETEC**) strains isolated from 1,211 children with diarrhea in Argentina. One hundred nine **ETEC** strains that were isolated from seven different laboratories in various regions of the country were tested for CFAs by using monoclonal antibodies against **CFA/I** and E. **coli** surface antigens **CS1**, **CS2**, and **CS3** of **CFA/II** and **CS4** and **CS5** of **CFA/IV**; a polyclonal antiserum against **CS6** was used. The CFAs searched for were found in 52% of the ETEC strains: 23% of the strains carried CFA/I, 17% carried CFA/IV, and 12% carried CFA/II. All of the CFA/I strains produced **heat-stable** enterotoxin, and several of them were of the prevalent serotypes O153:H45 and O78:H12. Among the 19 strains expressing **CFA/IV**, 16 expressed **CS5** and **CS6** and produced the **heat-stable** enterotoxin and most were of serotype O128:H21; the remaining 3 strains produced **CS6** only. No ETEC strains

expressing CS4 were found. Most (11 of 13) of the **CFA/II**-carrying ETEC strains expressed **CS1** and **CS3**, and 10 of them were of the O6:K15:H16 serotype and produced both **heat-labile** and **heat-stable** toxins. As many as 24 of the 109 CFA-negative ETEC strains gave mannose-resistant hemagglutination with erythrocytes from different species; 4 strains had high surface hydrophobicity, suggesting the presence of additional, as yet undefined, colonization factors in up to 25% of the ETEC isolates.

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ACCESSION NUMBER: 91131795 EMBASE
DOCUMENT NUMBER: 1991131795
TITLE: New adhesive factor (antigen 8786) on a human **enterotoxigenic** Escherichia **coli** O117:H4 strain isolated in Africa.
AUTHOR: Aubel D.; Darfeuille-Michaud A.; Joly B.
CORPORATE SOURCE: Bacteriologie-Virologie Serv., Faculte de Pharmacie,63001 Clermont-Ferrand Cedex, France
SOURCE: Infection and Immunity, (1991) 59/4 (1290-1299). ISSN: 0019-9567 CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB An **enterotoxigenic** Escherichia **coli** strain, E. coli 8786, of serotype O117:H4 produced only **heat-stable** enterotoxin and gave mannose-resistant hemagglutination with human and bovine erythrocytes. The strain adhered to the brush border of human enterocytes and to enterocytelike cell line Caco-2. Adhesion inhibition assays using Caco-2 cells with different adhesive factor extracts showed that the adhesive factor of E. coli 8786 is different from **colonization factor antigen I** (**CFA/I**), **CFA/II**, CFA/III of Darfeuille et al. (A. Darfeuille, B. Lafeuille, B. Joly, and R. Cluzel, Ann. Microbiol. Inst. Pasteur 134A:53-64, 1983), **CS6**, and antigen 2230. A bacterial surface protein, designated antigen 8786, with a molecular mass of 16,300 Da was responsible for the adhesion to intestinal cells. It was immunologically different from previously described adhesive factors as determined by immunoblotting. Antigen 8786 was detected on the bacterial cell surface and appeared to be nonfimbrial. NH2-terminal analysis of antigen 8786 showed no homology with the previously described adhesive factors. Nevertheless, antigen 8786 is closely related to the NH2-terminal sequence of Salmonella enteritidis fimbrin. A hybridization experiment using a synthetic oligonucleotide probe based on the NH2-terminal amino acid sequence of antigen 8786 revealed that the coding region was located on a 70-MDa plasmid.

L18 ANSWER 36 OF 39 MEDLINE on STN DUPLICATE 26

ACCESSION NUMBER: 88284919 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2456269
TITLE: Genetic control and properties of coli surface

antigens of colonization factor antigen IV (PCF8775) of **enterotoxigenic** Escherichia **coli**

AUTHOR: McConnell M M; Thomas L V; Willshaw G A; Smith H R; Rowe B

CORPORATE SOURCE: Division of Enteric Pathogens, Central Public Health Laboratory, London, United Kingdom.

SOURCE: Infection and immunity, (1988 Aug) 56 (8) 1974-80. Journal code: 0246127. ISSN: 0019-9567.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198808

ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19960129
Entered Medline: 19880831

AB **Enterotoxigenic** Escherichia **coli** producing **coli surface antigen 4** (**CS4**), **CS5**, and **CS6** of **colonization factor antigen IV** were examined. This factor was originally called putative colonization factor 8775 (PCF8775). All of the coli surface antigens were plasmid coded and were usually carried on the same plasmid as the genes coding for **heat-stable toxin (ST)** or **heat-labile toxin (LT)**; thus, CS5-CS6-**ST**, CS6-**ST**, and CS6-**LT** plasmids were found. In strains of serotype O25:H42, the genes coding for CS4 and CS6 were on a plasmid separate from that containing the genes coding for ST and LT. CS4 and CS5 were fimbrial antigens with a subunit molecular mass of about 17.0 and 21.0 kilodaltons (kDa), respectively. CS6 was found as a single polypeptide with a molecular mass of about 14.5 kDa in strains of serotypes O25:H42, O27:H7, and O27:H20 when heated extracts were run on sodium dodecyl sulfate-polyacrylamide gels. CS6-positive extracts of strains of serogroups O148, O159, and O167 showed two bands with molecular masses between 14.5 and 16.0 kDa.

L18 ANSWER 37 OF 39 MEDLINE on STN DUPLICATE 27

ACCESSION NUMBER: 86061603 MEDLINE

DOCUMENT NUMBER: PubMed ID: 3906040

TITLE: Properties of wild-type strains of **enterotoxigenic** Escherichia **coli** which produce colonization factor antigen II, and belong to serogroups other than O6.

AUTHOR: Scotland S M; McConnell M M; Willshaw G A; Rowe B; Field A M

SOURCE: Journal of general microbiology, (1985 Sep) 131 (Pt 9) 2327-33. Journal code: 0375371. ISSN: 0022-1287.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198601

ENTRY DATE: Entered STN: 19900321

Searcher : Shears 571-272-2528

Last Updated on STN: 19900321
Entered Medline: 19860122

AB **Enterotoxigenic** strains of Escherichia **coli**, which belonged to serogroups other than O6 and produced **colonization factor antigen II**, usually produced only coli **surface antigen 3** (**CS3**) and gave weak mannose-resistant haemagglutination of bovine erythrocytes. A non-autotransferring plasmid, NTP165, from a strain of E. coli O168. H16 coded for **heat-stable** enterotoxin, **heat-labile** enterotoxin and CS antigens. The CS antigens expressed after acquisition of plasmid NTP165 depended on the recipient strain: a biotype A strain of serotype O6. H16 expressed CS1 and CS3; a biotype C strain of serotype O6. H16 expressed CS2 and CS3; strain K12 and strain E19446 of serotype O139. H28 expressed only CS3. An exceptional wild-type strain, E24377, of serotype O139. H28 produced CS1 and CS3 when isolated; a variant of E24377 which had lost the plasmid coding for CS antigens produced both CS1 and CS3 after the introduction of NTP165.

L18 ANSWER 38 OF 39 MEDLINE on STN DUPLICATE 28
ACCESSION NUMBER: 86061056 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3934290
TITLE: Enzyme-linked immunosorbent assays for the detection of adhesion factor antigens of **enterotoxigenic** Escherichia **coli**.
AUTHOR: McConnell M M; Thomas L V; Day N P; Rowe B
SOURCE: Journal of infectious diseases, (1985 Dec) 152 (6) 1120-7.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198512
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19851230

AB Two hundred forty-four specimens of Escherichia coli isolated in Bangladesh and Thailand and identified as enterotoxin producers were tested for the presence of adhesion antigens by mannose-resistant hemagglutination, immunodiffusion, and enzyme-linked immunosorbent assays (ELISAs). Specific antisera to the antigens **colonization factor antigen** (**CFA**)**/I, CFA/II** (consisting of coli surface antigens [**CS**] **1**, 2, and 3), and putative colonization factor antigen (PCF) 8775 (consisting of **CS4**, 5, and 6) were used in immunodiffusion tests and ELISAs. The results showed that the antigens could be detected in more strains by ELISA than by immunodiffusion. Twenty-nine percent of specimens of E. coli from Thailand and 47% from Bangladesh carried an adhesion antigen. Many of the strains had lost the ability to produce enterotoxins. Forty percent of strains from Thailand and 64% from Bangladesh that were still enterotoxigenic carried adhesion factors. These antigens were found on strains with **heat-stable** or **heat-stable** and **heat**

-**labile** enterotoxin but not on strains producing only **heat-labile** enterotoxin. PCF8775 antigens were associated mainly with strains from Bangladesh, where 10 strains that produced only CS6 were detected.

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ACCESSION NUMBER: 84036630 EMBASE
DOCUMENT NUMBER: 1984036630
TITLE: Expression of plasmids coding for colonization factor antigen II (CFA/II) and **enterotoxin** production in Escherichia **coli**.
AUTHOR: Mullany P.; Field A.M.; McConnell M.M.; et al.
CORPORATE SOURCE: Division of Enteric Pathogens, Central Public Health Laboratory, London NW9 5HT, United Kingdom
SOURCE: Journal of General Microbiology, (1983) 129/12 (3591-3601).
CODEN: JGMIAN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 004 Microbiology
LANGUAGE: English

AB Two plasmids transferred from **enterotoxigenic** Escherichia **coli** (**ETEC**) of serotype O6.H16 and biotypes A and C coded for mannose-resistant haemagglutination (MRHA) and production of **heat-stable enterotoxin** (**ST**) and **heat-labile enterotoxin** (**LT**). Both plasmids were non-autotransferring being mobilized most efficiently by the R plasmid R100-1. They were similar in their genetic properties being incompatible with each other and plasmids of the Inc group FI. The wild-type strains produced the **colonization factor antigen II** (**CFA/II**) which was made up of different **coli** surface antigens (CS). The biotype A strains produced **CS1** and **CS3** while the biotype C strains produced **CS2** and **CS3**. These three antigens have the ability to cause MRHA. When plasmids coding for MRHA were transferred to K12 strains, the degree of haemagglutination was markedly reduced and only **CS3** was produced. When both plasmids were transferred back into biotype A strains, good MRHA was restored and the strains produced **CS1** and **CS3**. In a biotype C strain **CS2** and **CS3** were formed. The production of the antigens was compared by enzyme-linked immunosorbent assay (ELISA). The strains were also examined by electron microscopy where it was found that **CS1** and **CS2** were fimbrial antigens while **CS3** was not.

(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 11:42:54 ON 27 APR 2004)

- Author (s)

L19 292 S "CARLIN N"?/AU
L20 153 S "ASKELOF P"?/AU
L21 65 S "BJARE U"?/AU
L22 3 S L19 AND L20 AND L21
L23 5 S L19 AND (L20 OR L21)

Searcher : Shears 571-272-2528

L24 3 S L20 AND L21
L25 4 S (L19 OR L20 OR L21) AND L15
L26 6 S L22 OR L23 OR L24 OR L25
L27 3 DUP REM L26 (3 DUPLICATES REMOVED)

L27 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2000:441654 HCAPLUS
DOCUMENT NUMBER: 133:64009
TITLE: Oral vaccine against diarrhea
INVENTOR(S): **Carlin, Nils; Askelof, Per; Bjare, Ulf**
PATENT ASSIGNEE(S): SBL Vaccin AB, Swed.
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037106	A1	20000629	WO 1999-SE2306	19991209
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
SE 9804415	A	20000619	SE 1998-4415	19981218
SE 515285	C2	20010709		
BR 9916278	A	20010904	BR 1999-16278	19991209
EP 1140159	A1	20011010	EP 1999-964847	19991209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EE 200100309	A	20020815	EE 2001-309	19991209
JP 2002532562	T2	20021002	JP 2000-589216	19991209
ZA 2001004362	A	20020114	ZA 2001-4362	20010528
HR 2001000433	A1	20020630	HR 2001-433	20010608
NO 2001002889	A	20010612	NO 2001-2889	20010612

PRIORITY APPLN. INFO.: SE 1998-4415 A 19981218
WO 1999-SE2306 W 19991209

AB An oral vaccine composition against **enterotoxigenic** E. **coli** caused diarrhea in humans is disclosed. It comprises a defined amount of at least three different types of colonization factor antigens (CFAs), e.g. 100 to 300 μg of each type, selected from the group consisting of **CFA I, CFA II** (**CS1, CS2** and **CS3**) and **CFA IV** (**CS4, CS5** and **CS6**), on killed E. coli bacteria lacking the gene encoding the heat labile enterotoxin (LT-), together with a defined amount of the B-subunit of cholera toxin (CTB), e.g. 0.5-2.0 mg, and a vehicle, such as PBS, which vaccine composition is purified from possible heat stable enterotoxin (ST).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:468494 BIOSIS
DOCUMENT NUMBER: PREV199900468494
TITLE: Method of cultivating bacteria proteins that are expressed in a temperature regulated manner.
AUTHOR(S): **Askelof, Per** [Inventor, Reprint author]; **Carlin, Nils** [Inventor]; Nilsson, Bo [Inventor]; Paulsson, Agneta [Inventor]
CORPORATE SOURCE: Department of Clinical Research, Merck Sharp and Dohme (Sweden) AB, SE-192 07, Sollentuna, Sweden
ASSIGNEE: SBL Vaccin AB
PATENT INFORMATION: US 5935838 Aug. 10, 1999
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 10, 1999) Vol. 1225, No. 2. print.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Nov 1999
Last Updated on STN: 9 Nov 1999

L27 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 1996:87113 HCAPLUS
DOCUMENT NUMBER: 124:115558
TITLE: Method for culturing bacteria producing membrane-bound antigens expressed in a temperature-regulated manner
INVENTOR(S): Askeloef, Per; **Carlin, Nils**; Nilsson, Bo; Paulsson, Agneta
PATENT ASSIGNEE(S): SBL Vaccin AB, Swed.
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9533825	A1	19951214	WO 1995-SE628	19950601
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9526349	A1	19960104	AU 1995-26349	19950601
EP 759981	A1	19970305	EP 1995-921214	19950601
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1154716	A	19970716	CN 1995-194475	19950601

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CN 1117859	B	20030813			
JP 10501406	T2	19980210	JP 1995-500754		19950601
US 5935838	A	19990810	US 1997-750509		19970421
PRIORITY APPLN. INFO.:			SE 1994-1921	A	19940603
			WO 1995-SE628	W	19950601

AB A method of cultivating bacteria having genes in plasmids which code for surface or membrane bound antigens or other proteins and which are expressed in a temperature regulated manner for the production of desired bacterial products, is disclosed. The bacteria are first cultivated in a culture medium to an inoculum under such temperature conditions that the bacteria retain their plasmids and no expression occurs, e.g. 20°C, and then in a culture medium under such temperature conditions that expression occurs and before the bacteria lose their plasmids they are harvested, and the desired product is isolated. The product may be the bacteria or isolated antigens, either of which may be used as a vaccine. Thus, **enterotoxigenic** Escherichia **coli** (**ETEC**) expressing a colonization factor antigen such as **CFA/I** or **CS1** - **CS6** was cultured at 20°, then at 37°. When compared with ETEC cultured only at 20°, or only at 37°, the ETEC cultured at a lower temperature and shifted to the higher temperature produced more antigen. This was related to loss of a regulatory gene on a plasmid at the higher growth temps.

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